ABSTRACTS OF WORLD MEDICINE

VOL. 20 NO. 3 SEPTEMBER, 1956

Pathology

539. **The Pathology and Pathogenesis of Experimental Anaphylactic Glomerulonephritis in Relation to Human Acute Glomerulonephritis**

A. R. RICH. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **98**, 120–151, Feb., 1956. 26 figs., 46 refs.

Stating that "it has long been suspected that hypersensitivity may be an important determining mechanism in the pathogenesis . . . of human glomerulonephritis", the author describes experiments carried out at Johns Hopkins University, Baltimore, in which all the glomerular changes characteristic of human glomerulonephritis were demonstrated in rabbits which developed glomerulonephritis as the result of an anaphylactic hypersensitive reaction produced by antigens that had no primary toxicity. This was done by giving the animals one injection of sterile horse serum in a dose of 10 ml. per kg. body weight; they were killed 14 to 18 days later and the kidneys examined histologically.

It was observed that there was a latent period between the injection and the appearance of glomerular lesions corresponding to that required to permit a sufficient amount of antibody to be formed to clear the excess of injected antigen rapidly from the circulation. Occasionally lesions comparable with those associated with periarteritis nodosa in man were seen in the glomerular tuft.

The author discusses at some length the bearing of this experimental work on the pathogenesis of acute glomerulonephritis in human subjects. *E. G. Rees*

CHEMICAL PATHOLOGY

540. **Lipid Chemistry of the Brain in Demyelinating Diseases**

J. N. CUMINGS. *Brain* [*Brain*] **78**, 554–563, 1955. 11 refs.

Portions of white and grey matter from the brain in 3 cases of disseminated sclerosis, one of sudanophilic diffuse sclerosis, and one of metachromatic diffuse sclerosis were examined at the National Hospital, Queen Square, London, and their water, total phospholipid, mono-amino phospholipid, sphingomyelin, lecithin, cephalin, cholesterol, and cerebroside content estimated. In addition the neuraminic acid content and the acid-soluble, phospholipid, nucleic acid, and protein phosphorus content of these and of similar specimens from 2 more cases of disseminated sclerosis, 6 of amaurotic familial idiocy, and 4 of other types of diffuse sclerosis, and from 3 normal adults and one normal newborn baby were estimated.

The demyelinated areas in all cases showed a loss of phospholipid. The presence of cholesterol esters and the slight abnormality of the apparently normal areas previously reported in disseminated sclerosis was confirmed (Cumings, *Brain*, 1953, **76**, 551). Changes in the phosphoprotein phosphorus level were found which suggested that in the demyelinated areas there was an initial loss followed by a return to a more normal level such as is found experimentally in crushed nerves. The neuraminic acid values were above the normal level (140 to 180 mg. per 100 g. dry tissue) not only in amaurotic idiocy (260 to 360 mg. per 100 g.), but also in the other demyelinating diseases (184 to 375 mg. per 100 g.).

The author makes the suggestion that the chemical examination of biopsy specimens might prove useful in diagnosis, and an example of such an examination is given. *J. E. Page*

541. **Amino-acid Levels in Pleural Exudates**

M. SANDLER. *Thorax* [*Thorax*] **11**, 60–64, March, 1956. 2 figs., 24 refs.

In a study undertaken at the Brompton Hospital, London, to determine whether the amino-acid pattern in plasma or exudate could be correlated with a particular pathological condition, the amino-acids were estimated in specimens of pleural exudate (and, in 9 cases, of plasma) from 13 patients with a primary tuberculous complex, 4 with post-primary tuberculosis, 10 with bronchial carcinoma, and 5 with secondary carcinoma by means of two-dimensional paper chromatography. In this procedure the quantitative results can be assessed only approximately, and this was done by grading numerically from 1 to 10 the intensity and size of the ninhydrin colour reaction.

The investigation showed that the general amino-acid pattern of the pleural exudates was similar to that of plasma, although the amino-acid concentration in the exudates was lower. The author suggests that some absorption of amino-acids may take place in the tissues enclosing the exudate. There was a high correlation between the rise and fall of the concentrations of valine and of leucine, but there was no significant difference between the amino-acid pattern of the exudate in tuberculosis and that associated with neoplastic disease.

J. E. Page

542. **The Blood Ammonia in Normal Persons**
W. G. CALKINS. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 343–348, March, 1956. 3 figs., 9 refs.

It is usually thought that the circulating blood normally contains no ammonia and that ammonia found in blood specimens from healthy individuals had been liberated rapidly after the blood was shed. To test this theory the author has examined blood from 10 patients with no evidence of liver disease at the Medical Center of the University of Kansas, Kansas City. Within 10 seconds of being taken a sample of blood was run into a saturated solution of potassium carbonate, as required for the estimation of the blood ammonia content by Conway's method, and other samples were similarly treated at intervals of 20 to 180 seconds after taking. An appreciable amount of ammonia was present in all the 10-second samples and there was only an insignificant rise in level during the 180 seconds after shedding. When blood from 5 additional patients was examined at intervals of 3 to 60 minutes after shedding, however, a gradual rise in the ammonia concentration was noted, starting about 20 minutes after the blood was obtained.

The fact that there was no significant change in the blood ammonia concentration in these subjects during the first 20 minutes suggests that the amount present in the blood 10 seconds after shedding, which varied from 44 to 90 μg. ammonia nitrogen per 100 ml., was also present in the blood *in vivo*. *H. Lehmann*

543. **Diagnostic Significance of Changes in Free, Esterified and Protein-bound Cholesterol, Lipo- and Glycoproteins in Lymphoma and Multiple Myeloma**
S. I. MAGALINI, M. STEFANINI, and H. M. MARIN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 155–164, Feb., 1956. 4 figs., 19 refs.

Working at St. Elizabeth's Hospital (Tufts University School of Medicine), Boston, the authors have studied the extent and diagnostic significance of changes in the serum cholesterol level and the electrophoretic migration of serum proteins, protein-bound cholesterol, lipoproteins, and glycoproteins in patients with various types of lymphoma (31) and multiple myeloma (4), control observations being made on 5 healthy subjects before and after fatty meals and on 2 patients with parenchymal liver disease. Howe's technique was used for determination of serum protein and Durrum's method for the paper electrophoresis of proteins, lipoproteins, and glycoproteins. Schonheimer and Sperry's method was used at first for the determination of the total serum cholesterol content, but later a modification of Zlatkis's technique was employed. A new technique for the determination of electrophoretic mobility of protein-bound cholesterol was developed, in which a piece of Whatman No. 3 filter paper 2 inches (5 cm.) wide is divided by a pencil line into two strips $\frac{3}{4}$ and $1\frac{1}{4}$ inch (2 and 3 cm.) wide respectively, each of which is spotted with serum. Migration is obtained by Durrum's technique and the narrower strip is stained for protein by Durrum's method, the location of the various fractions being established spectrophotometrically with a 595-λ filter. After apposition of the two strips the larger one is cut transversely to separate the various fractions. Each section is then extracted three times with 3 ml. of a boiling acetone–alcohol mixture (50 : 50) and the eluates combined and desiccated overnight. The dry residue is then taken up in 2 ml. of pure acetic acid and the cholesterol content determined by Zlatkis's method.

In cases of lymphoma in relapse there was a characteristic decrease in the serum total cholesterol and cholesterol ester content, with a tendency to revert to normal during remissions. The serum total protein content was decreased in all active cases, usually with inversion of the albumin : globulin ratio. The α-globulin fraction was increased in all cases, the β- and γ-globulin fractions only occasionally. The protein-bound cholesterol level was increased in the albumin and, less constantly, in the α-globulin fraction, and was decreased in the β-globulin fraction, in all cases in relapse. Changes in the lipoproteins and glycoproteins followed a similar but less regular pattern. It is stated that these changes in the serum free, esterified- and protein-bound cholesterol levels are fairly typical of lymphoma and are found almost exclusively in the advanced stages of the disease. In multiple myeloma normal serum cholesterol levels were found normally distributed among the protein fractions, while lipoproteins and glycoproteins were preferentially associated with the pathologically increased protein fractions—changes similar to those occurring in liver disease.

The authors conclude that the behaviour of the serum protein-bound cholesterol level may be of some diagnostic value in lymphoma. *Victor M. Rosenoer*

544. **A Study by Paper Electrophoresis of the Serum-lipoproteins in Diabetic and Non-diabetic Subjects**
R. W. R. BAKER, C. L. JOINER, and J. R. TROUNCE. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 295–305, Oct., 1955 [received Jan., 1956]. 8 figs., 18 refs.

The authors have investigated at Guy's Hospital, London, the relative proportions of α and β lipoproteins in the serum of 80 diabetic patients and 50 non-diabetic subjects by means of paper electrophoresis; the paper strips were stained with light green for albumin and globulin and Sudan black for the lipoproteins and these fractions then assessed both visually and by means of a photometric scanner. For the purposes of this study a diagnosis of atheroma was made only if there was manifest coronary or peripheral vascular disease.

In all age groups the $\beta : \alpha$ lipoprotein ratio was higher in the diabetic than in the normal subjects; although the range of scatter was wide, the difference is regarded as significant. Comparison of the diabetic patients without atheroma with those with this lesion showed that the latter had a significantly higher mean $\beta : \alpha$ lipoprotein ratio than the former, although the scatter was again large. Also, obese diabetic patients aged over 50 were shown to have a significantly higher $\beta : \alpha$ ratio than obese non-diabetics of similar age. No significant relationship was found between duration of the diabetes and the $\beta : \alpha$ ratio. The significance of the findings is discussed. (The results are presented mainly in the form of diagrams.) *C. L. Cope*

545. **Serum Iron in the Diagnosis of Hepatobiliary Disease**
L. SCHAMROTH, W. EDELSTEIN, W. M. POLITZER, and N. STEVENS. *British Medical Journal* [*Brit. med. J.*] 1, 960–963, April 28, 1956. 3 figs., 25 refs.

The authors report an investigation into the diagnostic value of serum iron determinations which was carried out at the South African Institute for Medical Research, Johannesburg, on 63 patients with hepatobiliary disease. The normal range was taken as 70 to 185 μg. of iron per 100 ml., and increased values (>220 μg. per 100 ml.) were found in 19 out of 21 cases of infective hepatitis, all of 6 cases of subacute viral hepatitis, and 3 out of 8 cases of homologous serum hepatitis. On the other hand only in one (a case of portal cirrhosis) out of 28 cases of non-viral liver disease (including cirrhosis, gall-stone obstruction, carcinoma of the head of the pancreas, and chlorpromazine jaundice) was the serum iron level increased. There was no constant relationship between the serum iron level, the serum bilirubin level, and the severity of the disease in the former group. In 4 cases of viral hepatitis treated with daily intramuscular injections of 1 mg. of vitamin B_{12} (cyanocobalamin) there was a fall in the serum iron level on the second day.

They conclude that determination of the serum iron level is of value in the differentiation of viral hepatitis from extrahepatic obstruction and cirrhosis of the liver.
M. Lubran

546. **Simultaneous Determination of Cardiovascular–Renal Functions in Man by a Constant Infusion Technique**
C. H. HENDRICKS, E. J. QUILLIGAN, L. A. SAPIRSTEIN, A. J. PULTZ, and M. J. MANDEL. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **230**, 648–656, Dec., 1955. 12 refs.

Simultaneous studies were made of the cardiac output, renal function, and total body water in 10 healthy subjects at the Ohio State University Medical Center, Columbus, Ohio, by determination of the clearance of continuously infused mannitol and PAH. The method was as follows. Phenazone (1 g.) was administered intravenously at 7 a.m.; two hours later an arterial blood sample was taken and " priming doses " of 35 ml. of 25% mannitol and 5 ml. of 20% PAH were given. Immediately thereafter a constant infusion of 20% mannitol and 4% PAH was begun at the rate of 0·8 ml. per minute through a constant infusion pump for 35 minutes, brachial arterial blood samples being taken at 20, 25, 30, and 35 minutes. The infusion was then discontinued suddenly and further blood samples taken after 2, 4, 6, and 8 minutes. After the last sample was withdrawn 25 mg. of azovan (Evans) blue was injected rapidly and arterial samples collected at 2-second intervals for 60 seconds. A final blood sample was taken 10 minutes later and the arterial needle withdrawn. The plasma clearances of PAH and of mannitol were determined from the ratio between the infusion rate and the equilibrium concentration attained at the end of the infusion. The volume distribution of the two substances was also calculated from the slope of the disappearance curve on stopping the infusion, the latter representing the ratio between the clearance and the volume of distribution. Cardiac output was determined by the Fick principle and also by the azovan-blue method; plasma volume was also determined by the azovan-blue method, and from it total blood volume was calculated. The total body water was estimated from the antipyrin space.

Cardiac output as determined by the dye-dilution and by the stopped-infusion methods did not differ by more than 25% in any case and on the average agreed to within 1·5%; the average values for cardiac output of 7·54 and 7·44 litres per minute were somewhat higher than the usual reported figures for normal subjects of the same size and build. The volume of distribution of PAH averaged 14·5% of the body weight, compared with 16·4% for mannitol. The phenazone space was unusually large, ranging from 49 to 69·9% (average 60·3%) of body weight. The azovan-blue space ranged from 4·3 to 8·3% (average 7·13%) of the body weight. The plasma clearance of PAH averaged 633 ml. per minute and of mannitol 132 ml. per minute. The filtration fraction ranged from 0·153 to 0·284 (average 0·214). Certain limitations of the procedure are discussed.
Robert de Mowbray

547. **Specific Enzymatic Determination of Glucose in Blood and Urine Using Glucose Oxidase**
E. R. FROESCH and A. E. RENOLD. *Diabetes* [*Diabetes*] 5, 1–6, Jan.–Feb., 1956. 2 figs., 16 refs.

A relatively simple method for estimating glucose in blood and urine using the enzyme glucose oxidase is described in this paper from the Peter Bent Brigham Hospital (Harvard Medical School), Boston. The enzyme has a high degree of specificity for glucose, being totally inactive against fructose and galactose and only very slightly active against mannose and xylose. The daily urinary glucose excretion of 30 normal subjects ranged from 16 to 132 mg., with a mean of 72 mg. This represented only about 14% of the total reducing substances present in the urine. Glucose excretion was relatively independent of variation in the dietary carbohydrate intake, but a considerable increase in glucose excretion was detected after the administration of carbohydrate-active steroids.
H. Harris

548. **Uropepsin Excretion Studies in Clinical Surgery**
A. H. LEVY and S. LEVINE. *Gastroenterology* [*Gastroenterology*] 30, 270–278, Feb., 1956. 26 refs.

The authors have studied the 24-hour urinary excretion of uropepsinogen—a substance which on acidification is converted to a proteolytic enzyme probably identical with gastric pepsin—in 26 patients undergoing surgical treatment for peptic ulcer at the Veterans Administration Hospital, East Orange, New Jersey. Although 129 estimations were performed, the authors were unable to establish a satisfactory baseline of uropepsinogen excretion for any individual patient because of the sudden deviations from an apparently predictable level.

Of the 26 patients, 12 had gastric ulcer and were treated by gastric resection; when possible both pre- and post-operative estimations of uropepsinogen were carried out.

These showed that the operation was usually followed by a decrease in uropepsinogen excretion, but this decrease was not proportional to the amount of gastric tissue removed, some patients indeed excreting more enzyme after than before the partial gastrectomy. A further 7 patients with duodenal ulcer were treated by vagotomy and gastro-enterostomy; in these cases no effect of the treatment on uropepsinogen excretion could be demonstrated. The authors conclude that the uropepsinogen excretion is not a useful index of gastric secretory activity in surgical patients and that, contrary to previous reports, it is probably not proportional to the gastric secretion of pepsin. *M. J. H. Smith*

HAEMATOLOGY

549. **A Hemolysin Test for Selection of Universal Donors**

D. A. McDERMOTT and L. H. MUSCHEL. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **26**, 4–12, Jan., 1956. 12 refs.

To detect and measure the level in human serum of isoantibodies capable of effecting haemolysis, serum from 1,982 random samples of Group-O blood was incubated with erythrocytes of Groups A_1 and B, together with a complement control tube containing inactivated haemolytic reference serum and the corresponding erythrocytes together with the serum under test. In 55·2% of cases the serum was non-haemolytic or only weakly haemolytic, in 16·4% it was moderately haemolytic, and in 28·4% it was strongly haemolytic. Haemolytic activity was compared with isoagglutinin titre in 622 samples and a high correlation shown to exist, though there were many exceptions. A fairly high correlation of haemolytic activity with the result of the Coombs test was obtained in tests on 514 sera, but again marked disagreement in individual cases was not infrequent. A surprisingly large number of sera (about 30%) were found to contain isoagglutinins in high titre, and a further 15% contained isoagglutinins in low titre but were strongly haemolytic. The authors recommend the incorporation of a test for haemolysins in routine indirect blood grouping. *Marjorie Le Vay*

550. **Evaluation of Three Diagnostic Procedures for Systemic Lupus Erythematosus**

J. R. HASERICK. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 497–504, March, 1956. 1 fig., 14 refs.

The author has compared the sensitivity and accuracy of the three techniques which have been devised for the demonstration of the cellular aggregation which constitutes the lupus erythematosus (L.E.) phenomenon—namely, using the patient's bone marrow, using peripheral blood, and by incubation of L.E. serum or plasma with normal (dog) bone-marrow cells *in vitro*—in cases of atypical systemic lupus erythematosus at the Cleveland Clinic, Cleveland, Ohio.

In 33 of a total of 79 cases the results of one or more of these three tests were positive, that with peripheral blood being positive in 30, that with the patient's marrow in 24, and that with the patient's plasma and dog marrow in 19 (the lower figure here, it is suggested, may have been due to the use of heparin). All three methods have advantages and disadvantages, and these are discussed; the test with peripheral blood is the most sensitive, but at the same time is the most difficult to interpret. On the whole the author considers the plasma–dog-marrow method to be the most suitable for the following reasons: it allows a control to be set up, the test can be repeated several times with one specimen of serum, the serum can be sent long distances for examination if local facilities are inadequate, and it is the most suitable method for research. Replies to a questionary sent to 20 haemotologists in different regions of the U.S.A. showed that all but one of them considered the L.E. tests to be specific for systemic lupus erythematosus. *E. G. Rees*

551. **Some Factors Influencing the Formation of L.E. Cells. A Method for Enhancing L.E. Cell Production**

W. H. ZINKHAM and C. L. CONLEY. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **98**, 102–119, Feb., 1956. 5 figs., 12 refs.

In studies of the formation of L.E. cells *in vitro*, carried out at Johns Hopkins University School of Medicine, Baltimore, the authors have shown that the yield of L.E. cells from the blood of patients with systemic lupus erythematosus can be markedly increased if the blood is rotated in a flask containing glass beads during the incubation period. Experiments seemed to suggest that this is attributable to the effect of trauma on the leucocytes providing nuclear material for transformation, for as the degree of trauma to the leucocytes increased so, within limits, did the number of L.E. cells rise. The use of siliconed apparatus caused a marked reduction in L.E.-cell formation.

The authors also showed that large amounts of "extracellular material" may be produced by this technique, and the studies would seem to confirm that this material is derived from injured or dead leucocytes and is the primary stage in L.E.-cell formation. When this technique was employed in studying the blood of a large number of patients with collagen–vascular diseases other than systemic lupus erythematosus no L.E. cells or "extracellular material" could be demonstrated. *E. G. Rees*

552. **Rapid Procedure for Erythrocyte Packed Cell Volume and Sedimentation Rate Determinations**

V. RILEY and W. C. VALLES. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **91**, 341–347, Feb., 1956. 8 figs., 7 refs.

In the interests of convenience, speed, and economy the authors, working in New York, have devised a new method of estimating the packed erythrocyte volume and the erythrocyte sedimentation rate (E.S.R.). For this, relatively large-diameter (10 to 15 mm.) collection tubes and a solid coagulant (heparin or a mixture of ammonium and potassium oxalates) are used. With both estimations the need to transfer the samples of blood to a calibrated haematocrit tube is eliminated, the values

being read against a proportional volume chart which indicates as percentages the relative proportions of parts of a sample irrespective of its total volume. The E.S.R. is read at 30 minutes, after which the tubes are transferred to a suitable centrifuge. It is claimed that with this method, which has been used in testing more than 10,000 samples of blood, the time necessary for centrifugation is much reduced, and altogether the time taken to make the double estimation is cut by more than half. Comparison of the results on a quantitative basis with those obtained by conventional methods showed that the method gives approximately equivalent values and is sufficiently accurate for routine clinical use.

A. Brown

MORBID ANATOMY AND CYTOLOGY

553. **Lipid Metabolism in the Giant Cells of Certain Granulomata of the Skin.** (Über den Lipidenstoffwechsel in den Riesenzellen bei manchen Hautgranulomprozessen)

L. Popoff and N. Popoff. *Archiv für klinische und experimentelle Dermatologie* [*Arch. klin. exp. Derm.*] **202**, 238–246, 1956. 8 figs., 3 refs.

A careful survey, carried out at the Medical Academy, Sofia, Bulgaria, of 150 microscopical preparations of granulation tissue which had been differentially stained showed that the giant cells in tuberculous tissue contained many lipid granules, mostly arranged in the periphery of the cells. Some granules were also seen in the immediate neighbourhood of these cells.

It is suggested that this picture might be of differential diagnostic value, since it was seen only in tuberculous granulomata. In granulomata of the skin due to syphilis the giant cells showed only a small amount of lipid material, and this was diffused throughout the protoplasm of the giant cell. In some malignant granulomata of the skin the lipid was observed as a fine stippling both in and around the giant cells. In epulis and actinomycosis the giant cells were practically devoid of lipids. It is considered that the significant amount of lipid granules in tuberculous granulomatous tissues is closely connected with the metabolic needs of the tubercle bacillus.

G. W. Csonka

554. **Vascular Changes in Boeck's Sarcoid as a Sign of Hyperergic Inflammation of Tuberculous Aetiology.** (Über Gefässveränderungen beim Boeckschen Sarkoid als Zeichen einer hyperergischen Entzündung tuberkulöser Ätiologie)

G. Hebold. *Beiträge zur Klinik der Tuberkulose und spezifischen Tuberkulose-Forschung* [*Beitr. Klin. Tuberk.*] **115**, 184–202, 1956. 11 figs., bibliography.

This report from the Central Pathological Laboratory, Augsburg, describes the post-mortem findings in 3 cases of classic sarcoidosis and one in which it seemed likely that sarcoidosis had progressed to miliary tuberculosis. The author assumes [rather than proves] that the tubercle bacillus is the cause of sarcoidosis, basing his assumption largely on the histological similarity between the two diseases and on the occasional transition from sarcoidosis to frank tuberculosis. He describes in detail the essentially perivascular distribution of the granulomatous lesions of sarcoidosis (laying particular stress on early changes within the vessel wall, such as oedema and fibrinoid degeneration), draws attention to similar findings in frank tuberculosis, and gives his reasons for regarding such vascular changes as an expression of an allergic reaction to the tubercle bacillus or some of its constituents.

P. Mestitz

555. **Hyaline Membrane Diseases of Lungs. Further Observations**

M. J. G. Lynch. *Journal of Pediatrics* [*J. Pediat.*] **48**, 165–179, Feb., 1956. 10 figs., 31 refs.

In studies previously reported (Lynch and Mellor, *J. Paediat.*, 1955, **47**, 275; *Abstracts of World Medicine*, 1956, **19**, 262) the author attempted to show that hyaline membrane is formed from dried concentrated secretion of the respiratory bronchioles and alveolar ducts through the agency of enzymes. In a further investigation carried out at the General Hospital, Sudbury, Ontario, he has examined pulmonary hyaline membrane in man and experimental animals for dehydrogenases (by reduction of triphenyltetrazolium and potassium tellurite), for iron (by Perls's reaction after hydrogen peroxide and by dithizone followed by ammonia), and for haem (by treatment with hot caustic soda followed by ammonium sulphide, with subsequent microspectroscopy for the bands of haemochromogen) and here reports his findings.

Dehydrogenases were found in the lining of the respiratory tract from the respiratory bronchioles distally, and in the subendothelial layer of the pulmonary blood vessels; they were, however, absent from hyaline membrane. Organic iron was present in the lining of the respiratory tract, in hyaline membrane, and in erythrocytes. Haem was identified in all the above tissues, and also in the fluid of pulmonary oedema. In the post-mortem examination of many specimens of pulmonary tissue a well-marked hyaline membrane, containing free iron but no haem, was found in a patient dying of mitral stenosis who had received oxygen terminally.

Experimentally, hyaline membrane similar in its staining reactions to that seen in man was produced in rats, guinea-pigs, and frogs by exposure to high oxygen concentrations. In goldfish it was produced by adding hydrogen peroxide to the water. In the rats and guinea-pigs membrane formation was aided by the injection of pilocarpine, and although the animals were dyspnoeic and cyanosed after 24 to 48 hours, the lungs showed only small areas of oedema. After 48 to 84 hours hyaline membrane was seen in process of formation, apparently by the drying up of oedema fluid. The author suggests that haemosiderosis in mitral stenosis is not due to repeated focal haemorrhages, but rather to repeated episodes of hyaline-membrane formation as the result of drying up of oedema fluid.

[This paper contains some interesting observations, but in the abstracter's view the conclusions are based on rather tenuous evidence.]

M. C. Berenbaum

556. **Induration of the Hilar Lymph Nodes Due to Mixed Dust and its Relation to Cancer of the Lung.** (Mischstaubinduration der Hiluslymphknoten und Lungenkrebs)
H. GROSSE. *Frankfurter Zeitschrift für Pathologie* [*Frankfurt. Z. Path.*] 67, 220–231, 1956. 4 figs., bibliography.

After a brief review of the relevant literature, the author describes a comparative post-mortem study, carried out at the Institute of Pathology, Dresden, of induration of the lymph nodes associated with pneumoconiosis due to the inhalation of silica or mixed dust among 139 cases of pulmonary carcinoma and 322 in which no pulmonary neoplasm was present.

Of the 322 control cases, induration was present in 102. It was never found below the age of 49 years, and varied in degree, the early forms of induration involving the lymph nodes only and the late forms spreading into the neighbouring bronchi, the pulmonary vessels, and to an even greater extent into the bronchial vessels, which were often obliterated by fibrosis. In silicotic nodules softening was also present, and the histology in these cases is described in detail. This type of induration does not cause complete obstruction to the flow of lymph. Silicotuberculosis was present in some cases. Hilar induration was present in 68 of the 139 cases of carcinoma and presented no distinguishing features, except when the indurated nodes had been invaded or replaced by the tumour. The age incidence was about the same as in the control cases. In about one-half of the cases of carcinoma contralateral hilar induration from mixed dust was demonstrated histologically.

It is estimated that in at least one-third of the cases in this series carcinoma must have arisen in a lung free from hilar induration from this cause. Mixed dust, which includes many inhalants ranging from house and coal dust and smoke to arsenic, chromium, and other metals, cannot alone play a decisive role in carcinogenesis because both sexes are equally exposed to it, but it may well be a contributory factor in the presence of individual predisposition. *F. Hillman*

557. **The Thoracic Duct in Malignant Disease**
J. M. YOUNG. *American Journal of Pathology* [*Amer. J. Path.*] 32, 253–269, March–April, 1956. 13 figs., 24 refs.

The thoracic duct and left supraclavicular lymph nodes were dissected out and examined post mortem in 150 consecutive cases of malignant disease, including lymphoma but excluding leukaemia, multiple myeloma, and brain tumours. In 48 (37%) of the 129 cases of carcinoma and 12 of the 21 cases of lymphoma and sarcoma the thoracic duct was involved, while the left supraclavicular lymph nodes contained tumour tissue in the same number of the former group and in 16 of the latter. The point is made that the affected supraclavicular nodes are often not palpable during life, and that in cases of obscure intrathoracic and intra-abdominal neoplasms biopsy of these nodes may be helpful.

It is concluded that the thoracic duct is a very frequent and important pathway for the dissemination of neoplastic disease. *J. B. Wilson*

558. **Neurohistological Findings in Infantile Pylorospasm.** (Neurohistologische Befunde beim Pylorospasmus des Säuglings)
O. HAFERKAMP. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] 328, 239–248, 1956. 5 figs., 14 refs.

At the Pathological Institute of the University of Bonn the author studied the intramural nerve plexuses of the stomach in 9 infants, aged 4 to 7 weeks, with typical hypertrophic pyloric stenosis and in 4 infants of the same age without gastro-intestinal disorder who had died of pneumonia.

In addition to standard stains the author used the silver impregnation method of Bielschowsky–Gros and Feyrter's tartaric-acid–thionin technique. His findings confirmed those of Herbst, who described vacuolation of the nerve cells in the fundus, antrum, and pylorus in this condition, and he noted in addition the formation of lacunae in the nerve cells of the cardia. This change he calls "lacunar atrophy". The nerve bundles of the fundus and pylorus were often hyperplastic, showing fusiform swellings and fine, interwoven neurofibrils. The terminal intramural neurofibrils showed very severe regressive changes taking the form of granular disintegration.

The author points out that the relationship between these changes, which affect the vegetative nervous supply of the whole stomach, and the dysfunction and hypertrophy of the pylorus is far from clear. Moreover, even if it be assumed that pylorospasm is the primary cause of the obstruction and that it is directly attributable to the nervous changes, the aetiology of those changes remains in question. *H. S. Baar*

559. **The Degree of Coronary and Aortic Atherosclerosis in Necropsied Cases of Multiple Myeloma**
D. M. SPAIN, I. J. GREENBLATT, I. SNAPPER, and T. COHN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] 231, 165–167, Feb., 1956. 2 refs.

The authors have compared the degree of atherosclerosis found in the aorta and coronary arteries at necropsy at Beth-El Hospital, Brooklyn, New York, in 104 cases of multiple myeloma with that in two control series of 104 cases of cancer and 104 of accidental death. The average degree of atherosclerosis was significantly less in the first group (mean age 56 years) than in either of the control groups (mean ages 60 and 53 years respectively). Sex distribution was approximately the same in all three groups.

The authors relate this finding to the low serum cholesterol level found in 15 out of the 17 cases of multiple myeloma in which determinations had been made and to the rapid plasma clearance of lipid which occurs not infrequently in such patients.

[Confusion exists in the literature, the serum cholesterol level in multiple myeloma having been reported as normal, high, and low by different authors. Similar discrepancies exist in regard to protein-bound cholesterol distribution and lipoprotein distribution.]
Victor M. Rosenoer

560. **Gastric Lesions in Hodgkin's Disease and Leukemia**
H. R. WAHL and J. H. HILL. *American Journal of Pathology* [*Amer. J. Path.*] **32**, 235–251, March–April, 1956. 7 figs., 33 refs.

Out of a series of 64 cases of leukaemia examined at the University of Kansas School of Medicine, Kansas City, gastric lesions were present in 16, while out of 45 cases of Hodgkin's disease the stomach was involved in 9.

The gastric lesions in Hodgkin's disease varied a good deal, but tended to present as large, single or multiple, ulcerative masses, though diffuse invasive forms were also seen. In contrast the lesions in leukaemia were usually spread diffusely throughout the stomach wall with the formation of giant rugae—though here too nodular and ulcerated lesions might also occur. It is, however, emphasized that it is not possible to differentiate these two conditions on macroscopical examination of the stomach. Since Hodgkin's disease with large, ulcerated lesions is frequently mistaken clinically for a primary gastric neoplasm it is advisable to carry out a biopsy in all cases. *J. B. Wilson*

561. **Further Observations on the Morphology of Veno-occlusive Disease of the Liver in Jamaica**
G. BRAS and D. C. WATLER. *West Indian Medical Journal* [*W. Indian med. J.*] **4**, 201–211, Dec., 1955 [received April, 1956]. 9 figs., 36 refs.

Veno-occlusive disease of the liver is common in Jamaican children, and although recovery is frequent in the acute stage, it has been found that 47% of children of the poorer classes have some degree of hepatomegaly apparently attributable to this condition. The exact pathogenesis is still unknown, but a dietary deficiency of protein is probably the most important aetiological factor, while the consumption of " bush tea "—a decoction made from unspecified herbs from the jungle—may be a contributory factor.

The present authors describe the clinical and histological findings in 10 cases which they have selected from among the 19 which have come to necropsy at the University College of the West Indies to illustrate the acute and chronic phases of the disease. There were 8 males and 2 females and their ages ranged from 10 months to 16 years. The majority were in the chronic stage and had some degree of ascites, while in 4 cases the cause of death was haemorrhage from ruptured oesophageal varices.

In the acute stage the liver is congested and examination with a hand lens reveals thickening of the walls of the hepatic veins and, occasionally, thrombosis. Microscopically, the sinusoids are dilated and the parenchymal cells compressed, while the venous thickening is seen to be due to a subintimal deposit of loose reticular tissue with a few cells. In the later stages this becomes organized and the vein is permanently obstructed. There is centrilobular reticular proliferation leading to fibrosis and finally to non-portal cirrhosis. There are associated fatty changes in the liver resembling those seen in kwashiorkor. Although the gross appearances may suggest a nodular cirrhosis of the Laënnec type, it is important to note that the portal tracts are not affected in the first instance, the primary lesion being in the centrilobular vein. *William Hughes*

562. **The Pathogenesis of the Hyalinization of the Islands of Langerhans**
E. MOSCHCOWITZ. *A.M.A. Archives of Pathology* [*A.M.A. Arch. Path.*] **61**, 136–142, Feb., 1956. 5 figs., 34 refs.

In this communication from the Mount Sinai Hospital, New York, the author describes the post-mortem findings in the pancreas of 111 adult diabetic patients. In just under half the subjects fibrosis or hyaline change was present in the islets of Langerhans. The fibrosis, which is regarded as the forerunner of hyalinosis, begins as a pericapillary thickening of the basement membrane; later, the hyaline deposit widens and the islet epithelial cells are thus compressed and ultimately replaced, while the lumen of the capillaries is progressively narrowed but never entirely obliterated. These changes are nearly always associated with arteriosclerosis, being rarely found in patients under the age of 40 but rising sharply in incidence in those over that age. In a control series of 70 cases of essential hypertension similar islet lesions were present in 8 cases (11%)—an observation which accords with the known frequency of hyperglycaemia in this disorder. *A. Wynn Williams*

563. **The Basement Membranes of the Epithelium of the Colon and Rectum in Ulcerative Colitis and Other Diseases**
M. A. JACOBSON and J. B. KIRSNER. *Gastroenterology* [*Gastroenterology*] **30**, 279–285, Feb., 1956. 8 figs., 8 refs.

The purpose of the investigation here reported from the University of Chicago was to determine the frequency of changes in the basement membrane of epithelial cells of the rectum and colon, as seen on histological examination of biopsied or resected specimens of these organs from 136 patients suffering variously from ulcerative colitis, carcinoma, polyps, or regional enteritis.

A normal basement membrane was found in 22 out of 34 specimens taken from a " normal " area of colon, whereas the remaining 12 patients in this group, all of whom had carcinoma elsewhere in the colon, showed some degree of destruction of the basement membrane. Varying degrees of destruction were found in biopsy specimens removed from neoplastic areas of the colon in 43 out of 55 cases of carcinoma, in 4 out of 6 cases of regional enteritis, and in 7 out of 12 cases of polyp. The most extensive destruction of basement membrane was found in the group of 29 cases of ulcerative colitis, the changes being classified as " partial " in 7, " severe " in 10, and " complete " in 12. In general there appeared to be no consistent correlation between the degree of destruction of the basement membrane and the presence, absence, or severity of leucocytic infiltration at the site of destruction. The mechanism involved in these changes is unknown. It has been suggested that enzyme systems may be involved, but further work is necessary to elucidate this problem. *A. W. H. Foxell*

Microbiology and Parasitology

564. **Epidemiologic Studies on Antibiotic-resistant Strains of *Micrococcus pyogenes***

R. I. Wise, C. Cranny, and W. W. Spink. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 176–184, Feb., 1956. Bibliography.

A review of the literature has shown that antibiotic-resistant strains of coagulase-positive staphylococci are being encountered with increasing frequency in infections in patients and in the nasopharynx of apparently healthy staff in hospitals. It has also been noted that the incidence of antibiotic-resistant strains in the nasopharynx of hospitalized patients is roughly proportional to the duration of time spent in hospital, and is directly related to the quantity of the antibiotic used in that hospital.

In this paper from the University of Minnesota Hospitals, Minneapolis, the authors report the results of a comparative study of coagulase-positive strains of *Staphylococcus pyogenes* isolated from three different environmental groups at the hospitals. Coagulase-positive strains were found in 32·7% of 208 members of the hospital staffs, and in 20·5% of 200 out-patients. The third group consisted of 96 strains from 66 surgical patients who had infections.

The authors found that approximately 41% of the strains from the staff and in-patients were resistant to a concentration of 1,000 units of penicillin per ml. and only 19·1 and 5·2% respectively were sensitive to 1·0 unit per ml., whereas 60·9% of the strains from the out-patients were sensitive to 1·0 unit per ml. Resistance to a concentration of 1,000 μg. of streptomycin per ml. was found in 79% of the strains from in-patients and in 45% of the strains from the staff, but all the strains from the out-patients were inhibited by 1·0 to 100 μg. per ml. Tests with aureomycin (chlortetracycline) and oxytetracycline showed that 10 to 500 μg. per ml. was required to inhibit similar proportions of strains from the staff and in-patients, but 75 to 85% of the strains from the out-patients were sensitive to 0·1 to 1·0 μg. of these drugs per ml., and all strains were sensitive to 10 μg. per ml. Over 90% of the strains from all three groups were sensitive to 1·0 to 10 μg. of chloramphenicol per ml. and to 0·1 to 1·0 μg. of erythromycin per ml., while all the strains except 3·1% of those from the in-patients were inhibited by 10 μg. of bacitracin per ml.

The strains isolated from the out-patients were distributed through all the phage groups, but there was a predominance of Group III and of non-typable strains among those from the staff and in-patients. The authors conclude by stressing that the ubiquity of pathogenic, antibiotic-resistant strains of staphylococci in hospital environments indicates a great need for prophylactic measures to prevent cross-infection of patients and the establishment of the carrier state in members of the hospital staff.

A. Ackroyd

565. **The Demonstration of an Antibody against Complement**

A. P. McKee and W. S. Jeter. *Journal of Immunology* [*J. Immunol.*] **76**, 112–118, Feb., 1956. 1 fig., 16 refs.

The authors describe, from the State University of Iowa, a method whereby antibody to complement may be produced in rabbits by injecting bovine serum albumin antigen–antibody complex on which complement has been adsorbed. (Pig serum albumin, bovine gamma globulin, and egg albumen were also used with the appropriate antibodies.) Rabbits injected with such antigens showed typical primary and secondary responses to the complement they contained. Such antibodies to complement reduced the activity of homologous complement *in vitro*, gave weak cross-reactions with heterologous complement, and reduced the homologous complement activity of animal sera when they were injected intravenously. Addition of antibody to mixtures of homologous and heterologous complement appeared to remove both types of complement—the homologous complement by neutralization, the heterologous by adsorption—the amount of the latter removed being greater than could be accounted for by cross-neutralization.

C. L. Oakley

566. **Persistence of Antitoxin Levels after Tetanus-toxoid Inoculation in Adults, and Effect of a Booster Dose after Various Intervals**

J. M. Looney, G. Edsall, J. Ipsen, and W. H. Chasen. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 6–12, Jan. 5, 1956. 1 fig., 23 refs.

In a study of the serum antitoxin levels after tetanus immunization carried out at Boston University School of Medicine it was found that of 144 U.S. ex-service men who had been injected with tetanus toxoid between one and 10 years previously, all but 14 showed a level of more than 0·025 unit of tetanus antitoxin per ml. of serum; there was little apparent correlation between the residual titre and the interval since the last injection.

Of these subjects, 38 were given a single injection of 0·5 ml. of tetanus toxoid [concentration unstated] and 106 a single injection of alum-precipitated toxoid, blood samples from both groups being taken 6 days, between 14 and 21 days, and one year thereafter. Of 102 samples taken at 6 days only 4 had showed a concentration of less than 0·025 unit of antitoxin per ml., and of these, 2 reached satisfactory levels after one year, one was still below the lowest level tested, and no information was available about the fourth. All the remaining subjects tested had titres well above the presumed protective level, and this persisted in all but one of them for at least a year.

In the light of these findings the authors think that 4 years is a convenient interval between booster doses of tetanus toxoid, and that more frequent injections are unnecessary.

C. L. Oakley

Pharmacology

567. **A Chlorpromazine (Thorazine)-induced Cephalalgia and its Management**
S. E. ROBERTS. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **63**, 208–209, Feb., 1956.

Chlorpromazine is widely used and is usually well tolerated, but in the case here reported it caused excruciating headache, which was relieved only by administration of an antagonist. A woman of 33, who had undergone an operation for correction of spina bifida occulta, had some headache on being allowed to sit up, which was controlled with aspirin and codeine. She was then given 25 mg. of chlorpromazine 3 times a day for persistent paraesthesiae and the headache became unendurable. The usual analgesic drugs gave no relief, nor did pethidine or intravenous procaine or ergotamine with caffeine, but the injection of dihydroergotamine intravenously gave relief in half an hour. Two further doses of chlorpromazine were given, the first of which caused only mild pain, the second unbearable pain. This again was promptly relieved by dihydroergotamine, and there was no recurrence.

The most probable explanation is that chlorpromazine, which is a powerful vasodilator, is capable of producing a headache similar in intensity to the histaminic cephalalgia described by Horton, but without any remission; that the pain was reproducible and was completely relieved only by a powerful vasoconstrictor on each occasion strongly supports this view.

F. W. Watkyn-Thomas

568. **Changes in the Electroencephalogram, the Electrodermogram, and the Electromyogram Provoked by Chlorpromazine in Man.** (Modifications électro-encéphalographiques, électrodermographiques, et électromyographiques provoquées par la chlorpromazine chez l'homme)
M. TURNER, E. BÉRARD, N. TURNER, and N. FRANCO. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 25–34, Feb., 1956. 6 figs., 24 refs.

The effects of chlorpromazine on the electroencephalogram (EEG), electrodermogram (EDG), and electromyogram (EMG) were studied at the Laboratory of Clinical Electroneurophysiology, Buenos Aires, in 20 subjects, including cases of neurosis, psychosis, and epilepsy of various types. The activation procedures employed included overbreathing, photic, auditory, verbal, and nociceptive stimulation, and, in one case, leptazol injection. Chlorpromazine was injected intravenously in doses of 25 to 50 mg., injections of physiological saline being used for control purposes. It was found that intravenous chlorpromazine produced a greater degree of synchronization and regularity in the EEG, stabilized the EDG responses to sensory and nociceptive stimuli, and diminished activity in the EMG associated with such phenomena as involuntary movements and tremors. It is suggested that all these effects can be explained as due to action of the drug on the reticular system of the brain-stem. The use of chlorpromazine is proposed as an activating agent in some cases of epilepsy [? through its hypnotic properties] and as a means of eliminating muscle potentials and other artefacts from the EEG in cases complicated by involuntary movements.

William Cobb

569. **Changes in the Electrodermogram, in Sweating, and in Skin Temperature Provoked by Chlorpromazine ("4560 R.P.") in Man.** (Modifications de l'électrodermogramme, de la sudation et la température cutanée provoquées par la chlorpromazine (4560 R.P.) chez l'homme)
N. A. CLERC, M. TURNER, and E. BÉRARD. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 35–39, Feb., 1956. 3 figs., 13 refs.

The effects of chlorpromazine on the electrodermogram (EDG), on sweat secretion (measured by the Jadasshon–Manuila technique), and on skin temperature (measured with the MacKesson "dermalor") were studied in 5 subjects at the Laboratory of Clinical Electroneurophysiology, Buenos Aires. It is suggested on the basis of the results obtained that chlorpromazine has a central action, inhibiting the adrenergic secretion of sweat, abolishing the electrodermographic responses to activity, attention, mental effort, and emotion, which involve higher sympathetic reflex arcs, and inhibiting the central mechanism of vasomotor temperature regulation, as shown by a decrease in the difference between the skin temperature in the proximal and distal parts of the limbs.

William Cobb

570. **Studies of the Metabolism and Site of Action of "Aminazin" [Chlorpromazine] by Means of Radioactive Isotopes.** (Изучение методом меченых атомов распределения аминазина в организме и путей его выведения (Предварительное сообщение))
N. A. FEDOROV and S. Ē. SHNOL'. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **56**, 139–145, 1956. 6 figs.

Chlorpromazine labelled with radioactive sulphur (^{35}S) was prepared and doses of approximately 2 mg. per 100 g. body weight were given parenterally or by mouth to white rats. The animals were killed at varying intervals after the injection, and the radioactivity of various organs and tissues was determined. It appeared that chlorpromazine penetrated rapidly to all the tissues, reaching a peak concentration in 1½ to 2 hours with a relatively slow subsequent decline except in the blood, where the radioactivity rapidly fell to extremely low levels. The blood–brain barrier was passed without

difficulty, and the chlorpromazine concentration in the central nervous system was relatively fairly high. No pre-eminent site of accumulation within the central nervous system was found, but the content of the cerebral cortex was somewhat greater than that of other parts. The authors demonstrated significant differences between the tissue distribution of chlorpromazine and that of a number of other compounds studied by similar experimental methods.

Chlorpromazine administered parenterally was excreted unchanged by the kidneys, 97·4% being recovered in the urine in 4 days. When given by mouth only 16 to 17% was absorbed, the remainder being passed with the faeces in the course of 8 or 9 days, the delay being attributed to the local action of the drug on intestinal motility. *Alexander Duddington*

571. **Studies on Elorine Sulfate, an Anticholinergic Drug**

W. H. BACHRACH and H. SCHAPIRO. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 192–197, Feb., 1956. 1 ref.

The authors have investigated the physiological and clinical properties of the anticholinergic drug "elorine" sulphate (1-*cyclo*hexyl-1-phenyl-3-pyrrolidino-1-propanol methylsulphate; tricyclamol) in a series of tests on 150 individuals at the Veterans Administration Center (University of Southern California), Los Angeles.

Laboratory studies showed that the drug had a marked effect on reducing gastro-intestinal motility; it had no effect on the cephalic or gastric phase of gastric secretion, but did reduce basal and histamine-induced gastric secretion. In clinical studies carried out on 94 patients with various gastro-intestinal disorders (62 with peptic ulcer) the usual dose of the drug was 100 mg. four to five times daily. The authors suggest that 200 mg. at night should effectively reduce nocturnal gastric secretion. Dryness of the mouth was not a serious complication, but patients intolerant of other anticholinergic drugs were equally intolerant of elorine sulphate (about 10% of cases in this series). Of 52 patients with active ulceration who were treated with elorine and an intensive acid-neutralization regimen, 32 (60%) were completely relieved of symptoms, but recurrence was not delayed or prevented on discontinuation of the therapy.

G. S. Crockett

572. **Central Nervous System and Cardiovascular Effects of Rauwolfia Serpentina**

B. I. LEWIS, R. I. LUBIN, L. E. JANUARY, and J. B. WILD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 622–628, Feb. 25, 1956. 7 figs., 8 refs.

The effects of rauwolfia serpentina, in the form of "rauwiloid", its alseroxylon fraction, on the central nervous and cardiovascular systems were studied in 76 subjects, who were classifiable into three broad groups (some patients were included in more than one category, so that the sum of the groups exceeds the total number of subjects). Group 1 contained 50 patients with vascular and neurovascular syndromes, including hypertensive cardiovascular disease, coronary arterial disease with angina pectoris, and headaches with vascular symptoms due to states of tension; Group 2, 50 subjects with symptoms characterized as tension, anxiety, hysteria, and depression; and Group 3, 10 healthy subjects for comparison and study of certain pharmacological effects of the drug.

A daily dose of 4 mg. was found to be the most satisfactory in producing a therapeutic effect with the minimum of side-reactions. There was found to be no advantage in dividing the total dose, which was given at breakfast or bedtime. The mean fall in arterial pressure in all subjects was 19 mm. Hg; in 20 patients with essential hypertension the mean fall in pressure was 28 mm. Hg (range 7 to 53 mm.); among the 56 normotensive subjects remaining the mean fall was 14 mm. Hg (range 3 to 27 mm.). In general, the lower the original pressure the less was the fall during treatment. Bradycardia, with a mean slowing of heart rate by 19 beats per minute, was a more consistent feature than the reduction in blood pressure. The "tranquillizing" effect of the drug consisted in a general dulling and slowing both in mood and in motor activity. When some emotional tension was present this effect often resulted in "a relaxed sense of well-being", whereas those subjects who were less tense were more likely to feel dull and devoid of energy, with a deepening of depression, if present.

The pharmacological effects of the drug were not seen for some time after starting treatment, and persisted after it was withdrawn. In the 10 control subjects the onset of bradycardia was delayed for an average of 8 days. After medication was stopped the heart rate returned to normal in an average of 12 days, but the blood-pressure changes persisted for 20 days. The vascular effects of the drug were difficult to interpret. In the 20 hypertensive patients the clinical improvement was not related to the reduction in blood pressure. However, among patients with psychosomatic syndromes, all those with tension states improved, but not those suffering from depression or hysteria. *R. Wien*

573. **Clinical Experience with Acetyl-digitoxin: Preliminary Report**

M. GOLDFARB, M. C. THORNER, and G. C. GRIFFITH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 186–191, Feb., 1956. 8 refs.

The authors report the results of a clinical trial of acetyldigitoxin, produced by removal of one glucose molecule from lanatoside A, one of the glycosides of *Digitalis lanata*, in the treatment of 82 patients with congestive cardiac failure at Los Angeles County Hospital, California. The effect of the drug was quite satisfactory in all but 6 of the patients. It acted quickly and the side-effects, which occurred in about one-fifth of the patients, disappeared in one to 3 days on reducing the dosage.

The authors point out that although no attempt was made to compare acetyldigitoxin with other digitalis derivatives, the drug appeared to be at least equally effective. The average daily maintenance dose was 0·2 mg. given orally in tablet form. *G. S. Crockett*

Chemotherapy

574. **Laboratory and Clinical Studies with Nystatin in Post-antibiotic Mycotic Infections**
G. T. STEWART. *British Medical Journal* [*Brit. med. J.*] 1, 658–660, March 24, 1956. 2 figs., 5 refs.

The author has investigated the value of nystatin in the treatment of post-antibiotic mycotic infections. Studies carried out *in vitro* showed that in peptone and other liquid media nystatin inhibited the growth of typical strains of *Candida albicans* at concentrations of 5 to 20 units per ml., whereas on solid media concentrations of 20 to 40 units per ml. were required to achieve the same effect. Over 100 strains tested were sensitive to concentrations equivalent in liquid media to 5 to 20 units per ml. The inhibitory effect was maintained in the presence of plasma and serum, but only at higher concentrations; for example, in a medium containing 50% of serum, twice the concentration of nystatin was required. Cell division of *Candida* was completely inhibited by concentrations of 5 to 20 units per ml.; this was absolute, and raising the concentration to 100 units or more per ml. had no further effect.

In studies of the metabolic aspects of the action of nystatin on *Saccharomyces cerevisiae* the addition of 100 mg. of glucose per ml. to plain peptone media diminished the inhibitory effect on this organism by half. Maltose had less effect than glucose, but was more inhibitory than lactose. When the concentration of nystatin was raised to 40 or 50 units per ml. the inhibitory effect of glucose was lost. Combinations of nystatin with some fatty alcohols and glycols had an additive inhibitory effect without evidence of synergy. Aqueous suspensions of nystatin or solutions in organic solvents were unstable. An aqueous suspension kept at −20° C. for 2 weeks retained full potency, but losses up to 50% occurred in the dark, both at room temperature and at 37° C. In a series of passage experiments, strains of *C. albicans* and *S. cerevisiae* were exposed successively to 2, 6, and 50 units of nystatin per ml. for 48 hours without signs of lysis and without change in sensitivity to the original effective range of 2 to 12 units per ml. Nystatin had no effect on various strains of streptococci, staphylococci, and coliform bacilli. It did not inhibit the action of penicillin, the tetracyclines, chloramphenicol, or streptomycin on sensitive bacteria, nor did these antibiotics interfere with the action of nystatin on *Candida*.

In clinical trials the administration of 3 or 4 daily oral doses of 500,000 units of nystatin to 12 bronchitic patients, in whom moniliasis had developed as a sequel to antibacterial therapy, resulted in clearance of the sputum in 9 of them. Some effect was also obtained in 7 out of 8 cases of stomatitis, and a temporary effect in 2 cases of ringworm. Nystatin administered concurrently with antibacterial therapy to 18 patients had no definite prophylactic value in reducing the incidence of mycotic superinfection. Strains of *Candida* isolated during or after therapy showed no change in sensitivity to nystatin *in vitro*. Apart from transient nausea, no toxic effects were observed. *Norval Taylor*

575. **Evaluation of the Action of Nystatin on *Histoplasma capsulatum in vitro* and in Hamsters and Mice**
E. DROUHET, J. SCHWARZ, and E. BINGHAM. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] 6, 23–35, Jan., 1956. 5 figs., 8 refs.

In the investigation reported here from Cincinnati (Ohio) General Hospital nystatin (" mycostatin ") suspended in physiological saline and mixed with Sabouraud's glucose–agar medium was found to exert a fungistatic action *in vitro* on 14 different strains of *Histoplasma capsulatum* of American and African origin. It was noted that its activity was greater on the mycelial phase (14 strains) than on the yeast phase (8 strains).

In a further series of experiments *in vivo*, two on mice and two on hamsters (a species more susceptible to *H. capsulatum* even than mice), 50 mg. of nystatin was dissolved in 0·5 ml. of N:N-dimethylacetamide, diluted in 45·5 ml. of physiological saline containing 100 units of penicillin and 200 units of streptomycin per ml., and injected intraperitoneally. The mice were infected with a less virulent strain producing chronic disease, while the groups of hamsters received a moderately virulent and a highly virulent strain respectively, thus providing information on the effect of nystatin on fulminating, moderately acute, and chronic experimental histoplasmosis. Cultures from the liver and spleen of all the animals were examined.

Treatment in all cases was found to decrease mortality, inhibit dissemination of the disease in many animals, and effect sterilization of tissue in selected animals. If started after inoculation and after dissemination of the disease has occurred treatment should be given slowly and in progressively increasing dosage.

The authors conclude that nystatin is the first antibiotic to show unquestionable and constant effects on experimental histoplasmosis without producing toxic effects. *L. A. Elson*

576. **Entamide, a New Amoebicide. Preliminary Note**
N. W. BRISTOW, P. OXLEY, G. A. H. WILLIAMS, and G. WOOLFE. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] 50, 182, March, 1956. 1 ref.

577. **Methods for Determining the Sensitivity of *Mycobacterium tuberculosis* to Isoniazid, Streptomycin and PAS**
A. R. H. WORSSAM, P. COLLARD, J. D. CARROLL, and R. KNOX. *Tubercle* [*Tubercle (Lond.)*] 37, 73–80, April, 1956. 18 refs.

Infectious Diseases

578. **Sarcoidosis: Pulmonary and Skin Studies before and after ACTH and Cortisone Therapy**
A. SALOMON, B. APPEL, S. F. COLLINS, J. A. HERSCHFUS, and M. S. SEGAL. *Diseases of the Chest* [*Dis. Chest*] **29**, 277–291, March, 1956. 15 figs., 15 refs.

The effect of ACTH and cortisone in the treatment of 5 cases of sarcoidosis is reported from the Boston City Hospital. In all 5 cases there was evidence of generalized disease; the diagnosis was confirmed by the histological appearances of material obtained by skin biopsy in 3 cases and by mediastinal lymph-node and spleen biopsy in one each. The response to the Kveim test was also positive in 4 of the 5 cases. Pulmonary function studies revealed a slight diminution of lung volume in all the patients, but in none was there evidence of diffusion difficulty or disturbance of acid–base equilibrium.

ACTH gel was given to 4 patients and cortisone to one. There was regression of the sarcoid lesions in every instance, the response varying with the organ involved. Lesions of the skin, peripheral lymph nodes, parotid gland, and eyes responded most favourably. Marked amelioration of dyspnoea and cough was noted, but objective changes as revealed by pulmonary function studies were slight. *D. Geraint James*

579. **Cardiovascular Collapse in Acute Poliomyelitis**
J. A. HILDES, A. SCHABERG, and A. J. W. ALCOCK. *Circulation* [*Circulation* (*N.Y.*)] **12**, 986–993, Dec., 1955. 3 figs., 23 refs.

Among 1,359 cases of poliomyelitis admitted to the Winnipeg Municipal Hospitals the authors observed 28 cases of cardiovascular collapse, of which 22 were fatal. This complication occurred exclusively among the 523 in-patients with bulbar involvement and almost always within 48 hours of the onset of paralysis. It was never encountered in any of the 640 patients with only spinal paralysis, though there were 68 cases of respiratory failure among them. The temperature was 104° F. (40° C.) or higher in half the cases in which cardiovascular collapse occurred, the pulse was fast, regular, and of low tension, and the extremities were cold and clammy. A phase of hypertension preceded collapse in 10 instances. Clinical signs of gross pulmonary oedema appeared in more than one-third of the fatal cases a few hours before death. A continuous infusion of noradrenaline was of temporary benefit in 11 cases.

At necropsy, which was performed in 20 cases, there was no sign of obstruction of the airway. Histological examination of the nervous system showed varying degrees of medullary involvement in every case. Although the region between the floor of the fourth ventricle and the olivary nucleus was one of the most severely affected areas, the authors found "no apparent difference between the patients dying of cardiovascular collapse and those in which death was attributed to other causes". Histological evidence of interstitial myocarditis was found in 14 of the 20 cases and there was pulmonary oedema in all but one case.

Among the factors which might be primarily responsible for the development of this syndrome, destruction of the vasomotor centre, viral myocarditis, severe hyperthermia, adrenal insufficiency, prolonged positive-pressure breathing, and hypoventilation are all discussed but rejected, though in the case of hypoventilation the evidence for this rejection is admittedly incomplete. The explanation favoured by the authors is that there is a primary medullary lesion which causes severe vasoconstriction, thus accounting for the hypertensive phase; the hypertension then leads to the development of heart failure and pulmonary oedema, to which viral myocarditis contributes.

The clinical and pathological findings in the fatal cases and the clinical features of the 6 surviving cases are well presented in tabular form [but unfortunately biochemical examination of the blood was carried out in only 2 cases and no details are given of any electrocardiographic findings]. There is an excellent reproduction of a photomicrograph demonstrating the appearance of the interstitial myocarditis. *L. J. M. Laurent*

580. **Repeated Attacks of Scarlet Fever in Leningrad during 1951–1954.** (О повторных заболеваниях скарлатиной в Ленинграде в течение 1951–1954 гг.)
A. G. GRIGOR'EVA-BERENSHTEIN. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 82, No. 4, April, 1956.

The systematic treatment with penicillin of all patients suffering from scarlet fever was started in Leningrad during the second quarter of 1951, 200,000 units of penicillin being injected daily for 6 days. Of the total number of cases of scarlet fever which occurred between that date and October, 1954, 0·8% were second attacks. To determine whether this was attributable to penicillin two groups of patients were compared, one treated with penicillin and the other treated symptomatically, the incidence of second attacks being calculated per 10,000 patient-months of observation. The group treated with penicillin totalled 173,142 patient-months and the control group 522,567 patient-months. In the former group 269 children suffered from a second attack, that is, 15·5 per 10,000 patient-months, and in the control group 124 or 2·4 per 10,000 patient-months. In other words, second attacks were 6·5 times more frequent in the treated than in the control group. The majority (85%) of second attacks of scarlet fever occurred during the first year after the initial infection and were of shorter duration. It is emphasized that these findings should not be regarded as a reason for withholding penicillin in scarlet fever. Rather should they stimulate the search for methods of increasing the immunogenic stimulus in cases treated with penicillin. *K. Zinnemann*

Tuberculosis

581. **First Assessment of Systematic B.C.G. Vaccination in France.** (Premier bilan de la prévention systématique par le B.C.G. en France)
R. MANDE. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 130–139, Jan. 14, 1956. 3 refs.

The author presents the results of an unofficial inquiry into the working of the B.C.G. vaccination campaign in France, based on 49 of the 70 replies to a questionary sent by him to the Medical Officers of Health of the 89 departments.

Compulsory vaccination with B.C.G. for children born during the years 1938 to 1942 was started in France late in 1953, but in most areas did not begin until 1954 so that adequate information was available for only 49 departments. The proportion of children who actually attended for vaccination varied widely, ranging from 40% in some areas to 90% in others. It was estimated that the total number of tuberculin-negative children in the age groups concerned was over 1,000,000, but only 181,554 were reported as having been vaccinated up to March 1, 1955. The proportion of children in whom vaccination was considered to be contraindicated (and the criteria for this) varied greatly in different departments, in one case being as high as one-third. Vaccination was most often carried out by scarification and always with fresh vaccine, those to be vaccinated being selected on the result of a tuberculin test. Tuberculin conversion following vaccination was on the whole satisfactory, though there were exceptions to this; post-vaccination testing, however, was carried out with 50 T.U. of "I.P.48"—a much stronger test than usual. The incidence of complications, such as cervical lymphadenitis, following vaccination was extremely low, being only about one case in 2,000, while among the total of over 180,000 children vaccinated only 12 cases of primary infection in the weeks following vaccination were reported, some of which would doubtless have occurred if no vaccination had been given.

Discussing the comparatively poor response, the author attributes this less to resistance from the children's families—who on the whole accepted the obligation "with resignation"—but rather to lack of encouragement and explanation by those in charge of the scheme, and in certain cases to active opposition by some members of the medical profession. *T. M. Pollock*

582. **Current Results in Treatment of Tuberculous Meningitis and Miliary Tuberculosis**
J. LORBER. *British Medical Journal* [*Brit. med. J.*] **1**, 1009–1011, May 5, 1956. 1 fig., 5 refs.

In continuation of earlier reports (*Lancet*, 1954, **1**, 1104 and 1149; *Abstracts of World Medicine*, 1954, **16**, 292) the author now records his further experience in the treatment of tuberculous meningitis at the Children's Hospital, Sheffield. During 1954 20 patients were treated and all received systemic therapy with streptomycin and PAS as described in previous communications. In addition 5 patients were given a minimum of 45 injections of streptomycin intrathecally and 15 patients received a minimum of 25 such injections (average number 32). One child aged 3 years was admitted in an advanced stage of the disease and died within one week of admission without regaining consciousness—the only death in the series. One infant aged 4 months failed to progress on the standard treatment and developed hydrocephalus, but with addition of intrathecal tuberculin made a full recovery. One child relapsed 6 months after completing treatment, but with re-treatment on the same plan recovered, without sequelae.

After a period of observation ranging from 15 to 25 months 19 of the 20 patients are alive, 16 show no physical or mental sequelae, in 2 minimal hearing loss can be demonstrated only by audiogram, and one child, who had prolonged convulsions soon after admission, is a mentally defective hyperkinetic idiot. Unlike most workers in this field, the author still considers that intrathecal streptomycin is a necessary adjunct to systemic therapy despite the more speedy return of the cerebrospinal fluid to normal with fewer intrathecal injections and gives some cogent reasons for this point of view. He also reports that children suffering from miliary tuberculosis without meningitis were given the same systemic therapy as those with tuberculous meningitis. All 11 children so treated survived and none developed frank meningitis, although changes typical of "serous meningitis" were observed in some. A brief review of 69 patients with tuberculous meningitis treated at Sheffield during 1952–4, including those who died within a few hours of admission, shows that 59 (85·5%) survived.
R. M. Todd

583. **Development of Tuberculous Meningitis in Spite of Treatment with Isoniazid.** (Auftreten tuberkulöser Meningitiden trotz INH-Behandlung)
P. C. SCHMID and G. SCHOPPHOVEN. *Tuberkulosearzt* [*Tuberculosearzt*] **10**, 79–87, Feb., 1956. Bibliography.

While isoniazid is an effective agent in the treatment of tuberculous meningitis and there is evidence that its use has reduced the incidence of meningitis, the protection is not absolute and 8 cases are here reported from the Children's Sanatorium, Wangen-in-Allgau, Germany, in which involvement of the meninges developed in the course of, or immediately after, treatment with isoniazid for a primary complex (7 cases) or for tuberculosis of the ankle-joint following an earlier meningitis and involvement of the hilar lymph nodes (one case). There was no evidence that resistant organisms (whether developing in the course of treatment or acquired from other chemotherapeutically treated cases) were concerned. In all cases the infection was a severe one, but responded to combined treatment with isoniazid and streptomycin. *R. Crawford*

584. **The Value of Local Hydrocortisone in the Treatment of Tuberculous Cervical Lymphadenopathy.** (Traitement des adénopathies cervicales tuberculeuses. Intérêt de l'hydrocortisone locale)
R. A. MARQUÉZY, P. CHIGOT, J. VIALATTE, C. BACH, P. ESTÈVE, and P. GUIMBAUD. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 1111–1115, March 30, 1956.

The authors point out that despite the advent of chemotherapy the treatment of tuberculosis of the cervical lymph nodes is still unsatisfactory, and that the only real effect of antibiotics is to make surgery safer. They therefore decided to try the effect of local injections of hydrocortisone and here report their results in the treatment of 51 cases in children at the Hôpital Trousseau, Paris.

They divide their cases into two groups, primary and secondary, there being 35 in the former group and 16 in the latter. In Group 1 the portal of entry of the organism was determined in 20 cases and remained undiscovered in 15; the condition was unilateral in all 35 cases. In Group 2 the lesions were unilateral in 11 cases, bilateral in 3, and formed part of a general lymphatic tuberculosis in 2. Systemic chemotherapy was given first to nearly all the children, and local injections of antibiotics to 13; *x*-ray treatment was tried in 5 cases. The injection of hydrocortisone into the affected nodes was then undertaken in 11 cases, 10 mg. being given twice or thrice weekly. In 3 of these cases an antibiotic was given at the same time. The number of injections varied from 4 to 21 but all the patients were "cured" within 2 months. In 7, however, relapse followed; in 4 of these recovery followed a second series of injections, and in the other 3 chronic sinuses developed.

A preliminary trial of local hydrocortisone treatment is recommended in all cases of tuberculous cervical lymphadenitis before surgery is undertaken.

Wilfrid Gaisford

PULMONARY TUBERCULOSIS

585. **Incidence and Onset of Pulmonary Tuberculosis in Old Men**
E. G. WILKINS. *British Medical Journal* [*Brit. med. J.*] **1**, 883–886, April 21, 1956. 2 figs., 9 refs.

Notifications of respiratory tuberculosis in England and Wales from 1938 to 1954—calculated per 100,000 persons in each age group to nullify the effect of changes in the age structure of the population—showed a rise in the rate from 50 to 80 per 100,000 for men over 65 years of age, whereas the average yearly rate for women of this age remained steady at about 17 per 100,000. In contrast, the rates for both sexes aged between 45 and 65 remained constant in this period, while the rates for those between 15 and 45 years of age declined. The author shows that about one-third of the rise in notifications for men over 65 can be attributed to better detection by mass radiography. Of those discovered by this means, the proportion of active cases remained steady at 0·47% for older men, but declined over the period from 0·27 to 0·14% for older women. In the period 1938–54 the mortality from respiratory tuberculosis among women over 65 declined from 22 to 13 per 100,000, but for men of this age it rose from 58 per 100,000 in 1938 to a peak of 81 in 1951, and at 66 per 100,000 in 1954 is still 14% higher than in 1938. By 1954, the mortality and notification rates for males over 65 were about five times greater than for females.

The author then discusses the mode of onset as seen in 35 men admitted to Dorking General Hospital, Surrey, all of whom were well during their working lives and first developed symptoms of tuberculosis after the age of 65. Of these, 19 presented with chest symptoms, but the remainder had either no symptoms or only general symptoms, such as those of an intercurrent infection. In only 4 cases was the disease confined to one radiological zone. The author considers that most of these cases were due to reactivation of an old lesion, though only in one-half were there obvious medical or social predisposing factors. Constitutional disturbance in the elderly is often slight: the value of radiography and examination of sputum and blood (particularly for anaemia) is therefore emphasized. *J. N. Agate*

586. **The Treatment of Human Pulmonary Tuberculosis with Cycloserine: Progress Report**
I. G. EPSTEIN, K. G. S. NAIR, and L. J. BOYD. *Diseases of the Chest* [*Dis. Chest*] **29**, 241–257, March, 1956. 5 figs., 3 refs.

Cycloserine, a new broad-spectrum antibiotic, has been used at the Metropolitan Hospital (New York Medical College), New York, in the treatment of 57 patients with pulmonary tuberculosis. There were 25 acute cases previously untreated, and 32 cases of chronic infection which had become resistant to other antimicrobial agents. The treatment was discontinued for various reasons in 8 of the latter group. Crystalline cycloserine was administered by mouth in capsules, 20 to 25 mg. per kg. body weight (1·0 to 1·5 g.) being given daily in 4 doses over periods of 5 to 40 weeks.

In the acute cases symptomatic improvement was evident within 3 to 21 days of starting treatment. Occasionally there was an initial increase of fever, followed by a rapid return to normal after a few days except in cases of far-advanced caseous disease, which required up to 3 weeks to regain normal temperature. The appetite improved and weight gains of as much as 55 lb. (25 kg.) were recorded. Cough lessened progressively and sputum conversion occurred in all but 3 patients with far-advanced, bilateral, cavitating disease. Radiological improvement was marked, especially with prolonged treatment, complete clearing occurring in several cases. Symptomatic improvement occurred in all the chronic cases except for one patient with severe pulmonary fibrosis and emphysema. The gain in weight and strength and improvement in mental outlook were marked, and a number of patients became ambulatory after being bedridden for many months. Cough and sputum were reduced, with conversion in all except 7 cases of markedly atelectatic, bronchiectatic, and cavitary disease. Radiological improvement was "marked" in 5 cases, "moderate" in 13, and minimal or absent in 6. Old cavities decreased in size and their fibrotic walls gradually thinned out, making delineation difficult.

Transient side-effects of the drug which were observed included insomnia, dizziness, sleepiness, hyperirritability, increased reflexes, involuntary tremors, and skin rashes. Administration of the drug had to be discontinued owing to psychotic reactions in 3 cases and epileptiform manifestations in 2. There were no changes attributable to the drug in the blood, urine, or electrocardiogram, and the results of liver and kidney function tests were unaffected. No evidence was found of the development of resistance in tubercle bacilli exposed to cycloserine either *in vivo* or *in vitro* during the 10 months of this study. *I. Ansell*

587. **Preliminary Clinical Observation on the Treatment of Pulmonary Tuberculosis with Pyrazinamide.** (Prime osservazioni cliniche sul trattamento della tubercolosi polmonare con pirazinamide)
G. Daddi, M. Corda, C. Grassi, and F. Basilico. *Giornale italiano della tubercolosi* [*G. ital. Tuberc.*] **10**, 3–10, Jan.–Feb., 1956. 8 figs., 15 refs.

At the Phthisiological Clinic of the University of Milan the authors have treated 30 patients suffering from pulmonary tuberculosis with pyrazinamide, which was given alone for 30 consecutive days in a dosage of 2·5 g. daily. Toxic effects occurred in 6% of cases, but were mild. [Jaundice is not mentioned.] Most of the patients were generally improved, with less toxicity and a gain in weight, and most became sputum-negative, including several who had previously been resistant to isoniazid, while marked radiological improvement occurred in a number of cases. In 8 in which the sputum was still positive for tubercle bacilli after this treatment the organisms showed resistance to pyrazinamide in varying, but mostly high, degrees. The authors conclude that the drug is of definite promise in the treatment of pulmonary tuberculosis. *Arnold Pines*

588. **The Place of the Pituitary–Adrenal Hormones in the Treatment of Tuberculosis.** (La place des hormones hypophyso-surrénales dans le traitement de la tuberculose)
R. Even, C. Sors, A. Delaude, J. Roujeau, Y. Trocmé, and G. Commare. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **19**, 1249–1302, Dec., 1955 [received April, 1956]. 15 figs., bibliography.

This study of the combination of hormones with antibiotics in the treatment of pulmonary tuberculosis is divided into three parts, dealing respectively with clinical, pathological, and experimental findings.

In the first part the results obtained with ACTH (corticotrophin), cortisone (or hydrocortisone), or pituitary somatotrophic hormone (given in only 10 cases) in association with antibiotic treatment in 158 cases of secondary tuberculosis (54 pleural and 104 pulmonary) and 2 of primary infection (one pulmonary, one bronchial) are reported. The acute form of tuberculous pleurisy responded more favourably to the systemic administration of cortisone or ACTH than did the subacute or chronic type, but the authors emphasize that early treatment is essential if the full effect of hormone therapy is to be realized. The great majority of the 104 cases of pulmonary tuberculosis were treated with intravenous infusions of 10 mg. of ACTH daily for 3 weeks, each infusion lasting a minimum of 8 hours, together with antibiotics and a standard salt-free diet. Out of 86 acute and chronic cases so treated and 8 treated with cortisone the results were judged to be "good" in 37 and "fair" in 32, while 25 showed temporary improvement or none at all. The successful treatment is recorded of one case of massive hilar lymphadenitis and one of endobronchial tuberculosis. In the second part an account is given of a study of the anatomical modifications produced by the combination of hormonal with antibiotic treatment in 13 excised lungs or lung segments, from which the authors conclude that ACTH and cortisone, while inhibiting non-specific exudative processes, promote to the highest degree the action of antibiotics. In the third part a critical review of previous experimental work precedes an account of the authors' own experiments on guinea-pigs, in which they demonstrated that when hormones and antibiotics are given together in normal doses the results are superior to those obtained with antibiotics alone.

The authors plead for the adoption of a concept of tuberculosis which is less tied to the bacillus and takes fuller account of the non-specific tissue factors which govern the course of the infection. They maintain that the essential action of ACTH or cortisone on tuberculous inflammation is in the reduction or suppression of histologically non-specific exudative lesions, and that treatment should be directed simultaneously to accelerating fibrosis in the specific lesions and to eliminating non-specific exudative processes so far as possible, the latter object being achieved far more rapidly and effectively with ACTH or cortisone than with antibiotics. Such treatment is suitable for all forms of tuberculous inflammation which are both recent and progressive, but in the treatment of chronic disease the combined therapy should be reserved for serous lesions, for cases of pulmonary disease with intolerance of antibiotics, and for those severe cases which may by this means be made suitable for surgical intervention.
Norman F. Smith

589. **Surgical Treatment in Tuberculosis Complicated with Pulmonary Emphysema**
R. W. Newman, P. M. Huggin, C. L. Butler, and M. C. Bowman. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **31**, 125–137, Feb., 1956. 2 figs., 22 refs.

This paper from the East Tennessee Tuberculosis Hospital, Knoxville, compares the complications and morbidity following the surgical treatment of pulmonary tuberculous lesions in 30 patients with moderate to severe emphysema and 259 patients without significant emphysema. All had preliminary chemotherapy for periods ranging from 6 to 24 months, and in some cases temporary collapse measures were used. The sputum was negative for tubercle bacilli at the time of operation in about 75% of the cases.

Complications were much more numerous and more severe in the emphysematous group, broncho-pleural fistula (defined as an air-leak persisting longer than 7

days and associated with delayed re-expansion) occurring after 20 out of 26 resections (76·8%), and empyema after 5 (19·2%); there were 2 deaths (6·6%). In the non-emphysematous group broncho-pleural fistula occurred in 10% of cases and empyema in 3·9%; there were 8 deaths (3·1%). Protracted air-leaks from the raw surface of the lung constituted a major problem in the emphysematous group, as prolonged drainage was required and the risk of empyema was correspondingly increased.

The pathology of emphysema and the physiological and metabolic changes associated with it are discussed. Resection should be advised very cautiously in its presence, and alternative forms of treatment (such as Monaldi drainage followed by thoracoplasty and extraperiosteal plombage) which are better tolerated should be considered. If resection is necessary a small preliminary thoracoplasty (2 or 3 ribs) helps to reduce complications. The combination of a reduced maximum breathing capacity and a low timed vital capacity in a patient with obstructive emphysema is a very poor prognostic index and contraindicates resection. The operative management of these cases is discussed and the importance of relieving bronchospasm and of controlling paradoxical respiration is stressed. Tracheostomy at the time of surgery is valuable in eliminating some of the dead space, facilitating aspiration of secretions and controlling paradoxical respiration.

F. J. Sambrook Gowar

590. **Surgery for Cavitary Tuberculosis in Patients with a Single Lung**

F. M. Woods, N. J. Wilson, and R. H. Overholt. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **31**, 140–145, Feb., 1956. 3 figs.

The object of this short report from the Overholt Thoracic Clinic, Boston, is to show that resection is feasible when, after pneumonectomy, limited tuberculous disease in the remaining lung fails to respond to chemotherapy. The authors' experience with collapse therapy and cavity drainage in such cases has not been encouraging. Six cases are reported in which limited resection was carried out. There were 5 female patients and one male, their ages ranging from 24 to 48 years (average 36). The adequacy of their respiratory function for operation was assessed by clinical examination, and particularly from their ability to sustain ordinary activity without dyspnoea. The portion of lung resected was the right upper lobe in 2 cases and the right upper posterior segment, right apical lower segment, right apical lower sub-segment, and left apical lower segment with a wedge of the left upper anterior segment in one case each. Contralateral pneumonectomy had been carried out 18 months or more previously. Operation was performed with the patient prone, and anaesthesia was induced with cyclopropane followed by ether and oxygen. Care was taken to restore the stability of the chest wall by interlocking and suturing any divided ribs.

All 5 females survived, of whom 4 had an uneventful convalescence and are now sputum-negative and able to live a normal life; the fifth was 4 months pregnant at the time of her resection and a late air-leak occurred on the 7th postoperative day; her sputum is still intermittently positive, but she is able to lead a restricted home life. The only male (aged 48) underwent a right upper segmental resection and died on the 4th postoperative day with an air-leak and atelectasis.

These operations are better tolerated by younger patients and on the right side, because the larger size of the right lung gives a greater margin of safety. The remaining lung tissue must be healthy, with little or no nodulation or emphysema. [It is noteworthy that 5 of the 6 operations were on the right lung; although the patient who died was the only male in the series, he was also the oldest of the 6.]

(In a footnote a further case is reported—that of a man of 63 who had a right pneumonectomy for adenocarcinoma in August, 1950, followed by a successful resection of the apical-posterior and anterior segments of the left upper lobe for squamous-cell carcinoma in February, 1955.) *F. J. Sambrook Gowar*

591. **Advanced Pulmonary Tuberculosis with Persistent Cavitation. Preliminary Report on Prolonged Chemotherapy**

A. C. Douglas and N. W. Horne. *British Medical Journal* [*Brit. med. J.*] **1**, 375–378, Feb. 18, 1956. 6 figs., 24 refs.

Prolonged chemotherapy was given at the City Hospital, Edinburgh, in 6 cases of advanced pulmonary tuberculosis with gross cavitation, in all of which surgical treatment was impracticable by reason of the patient's age, the extent of the disease, or respiratory insufficiency. In 5 cases treatment consisted initially in 1 g. of streptomycin and 200 mg. of isoniazid daily; later 12 or 20 g. of PAS and 200 mg. of isoniazid were given daily for maintenance purposes. In the remaining case oxytetracycline and isoniazid were administered initially and streptomycin with isoniazid later. All patients were still receiving chemotherapy at the time of the present report. There was early clinical and radiological improvement in all cases, although cavities persisted. The sputum became negative within 2 months in 5 cases and within 5 months in the patient given oxytetracycline, and remained negative in all cases for 16 to 35 months. The authors state that the patients have been able to return to more or less normal life. No toxic effects were observed; in one case a mild upper respiratory tract infection developed on one occasion after discharge from hospital. *P. Mestitz*

592. **Direct Tracheal Lavage for Rapid Recovery of *Mycobacterium tuberculosis* from the Respiratory Tract**

J. S. Jones. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **50**, 176–180, April, 1956. 10 refs.

593. **Pulmonary Tuberculosis Simulating Bronchogenic Carcinoma**

N. S. Dontas and J. G. Callanan. *British Journal of Tuberculosis and Diseases of the Chest* [*Brit. J. Tuberc.*] **50**, 187–191, April, 1956. 3 figs., 14 refs.

Venereal Diseases

SYPHILIS

594. Failure to Prevent Congenital Syphilis

S. M. LAIRD. *British Medical Journal* [*Brit. med. J.*] 1, 768–772, April 7, 1956. 2 refs.

In the author's view congenital syphilis can be prevented by adequate antenatal treatment of the syphilitic pregnant woman. However, during the 5-year period 1950–4 in the area covered by the Manchester Regional Hospital Board, where there is an estimated total population of almost 4½ million, congenital syphilis was diagnosed in 139 children under 5 years of age. To determine the possible causes of failure to prevent the disease the records of these children and of their mothers were studied in detail. Some 30 cases were excluded because the diagnosis was based on the results of neonatal tests or tests on cord blood in which no allowance had been made for the "spill-over" of maternal reagin to the infant's circulation.

In 75 of the cases the mother had not undergone any antenatal serological test, the infection being discovered when signs of the disease developed in the infant or when serological tests were carried out on the mother in a subsequent pregnancy or as a possible family contact. Of these 75 mothers, 10 had previously defaulted during antisyphilitic treatment, 3 had each lost a child from syphilitic infection, and one had had a stillbirth the cause of which was not investigated, while the husband of another had been treated for secondary syphilis but had refused to bring his wife to the clinic for examination. Thus, 15 of the cases could have been prevented if an adequate history had been obtained, even although no antenatal test was performed.

In 34 cases a blood test was carried out during the antenatal period, and failure to obtain a healthy child was due to the following: (1) treatment begun less than 3 months before delivery (16 cases); (2) mother defaulted after treatment started (6 cases); (3) no action taken although the response to the blood test was positive (2 cases); (4) treatment refused (1 case); (5) test carried out too late for treatment to start before delivery (3 cases); and (6) negative response to antenatal blood test.

Discussing the findings, the author points out that many of these cases of congenital syphilis could have been prevented if a blood test had been carried out as a routine during the antenatal period. In some cases, however, the maternal infection was discovered too late for treatment to be effective, or premature labour or default of the patient reduced the time available for antisyphilitic treatment. Closer liaison between the maternity services and the venereologist might reduce the number of such cases. The problem of insensitivity of the standard serological tests for syphilis is a complex one, and it is suggested that in each case at least two tests should be performed, preferably in a central serological laboratory, in order to secure as high a standard of specificity as possible. *Benjamin Schwartz*

595. Calcification of the Aorta as an Aid to the Diagnosis of Syphilis

J. S. MCCANN and D. C. PORTER. *British Medical Journal* [*Brit. med. J.*] 1, 826–827, April 14, 1956. 6 figs., 11 refs.

Although radiological recognition of calcification of the ascending portion of the aortic arch is well known to be suggestive of syphilitic aortitis, the authors believe that insufficient attention has been paid to this sign. In this paper from the Royal Victoria and Women's Hospitals, Belfast, they review 19 cases of syphilis in which the sign was present. Of the 19 patients, of whom 13 were men and 6 women and whose age varied from 51 to 75, only 9 complained of symptoms related to the cardiovascular system, these having been present from 4 months up to 10 years. The duration of infection was not known in all cases, but appeared to extend from about 20 to 42 years.

Standard serological reactions for syphilis were positive in only 12 cases, and in 5 remained positive in spite of treatment. Radiologically, there was evidence of calcification in the ascending aorta in all cases; in 10 it was confined to the ascending aorta, in 6 it extended into the aortic valve, and in 9 it involved other parts of the aortic arch. Aneurysmal widening was present in 4 cases. The authors express the view that whether or not calcification due to atherosclerosis is present in the aortic valve or in the more distal parts of the aortic arch, "calcification of the first part of the ascending aorta is highly suggestive of an underlying or predisposing syphilitic lesion". *A. J. King*

596. Cardiovascular Disease in Syphilis

W. V. MACFARLANE, W. G. A. SWAN, and R. E. IRVINE. *British Medical Journal* [*Brit. med. J.*] 1, 827–832, April 14, 1956. 13 refs.

In this article are described the results of cardiological examination of 1,330 patients suffering from syphilis and seen at the General Hospital, Newcastle upon Tyne, during the period May, 1945, to December, 1951. In the investigation, which included physical examination, cardioscopy, and electrocardiography, 969 patients were examined before antisyphilitic treatment was given, 79 during such treatment, and 282 during surveillance after treatment. Those who showed signs of cardiovascular involvement were re-examined each year, if possible, up to 1954.

Of the total number of patients, of whom 676 were men (average age 47) and 654 were women (average age 43), 163 were suffering from early contagious syphilis, 265 from neurosyphilis, 780 from late syphilis which was

either latent or involving systems other than the nervous system, and 97 from congenital syphilis; the remaining 25 were examined because they gave a past history of syphilis. Evidence of cardiovascular syphilis was found in 202 patients (15%), 66 of whom were also suffering from neurosyphilis and 132 from other types of late syphilis. Of the remaining 4 patients, one was found to have aortic incompetence 4 years after apparently successful treatment of secondary syphilis. Fluoroscopy showed no abnormality of the aorta, and the diagnosis of syphilitic aortitis was based on the presence of aortic incompetence [a conclusion which is open to question]. Of 3 patients with congenital syphilis who were considered to have cardiovascular lesions, in only one was the evidence clear that the abnormalities found were due to the syphilis.

Syphilitic cardiovascular disease was commoner in men (143 cases or 70%) than in women (59 cases or 29%). Of these 202 cases, 45 were considered to have evidence of uncomplicated aortitis, 124 of aortic incompetence, 31 of aortic aneurysm, and 2 of syphilitic heart block. The incidence of aortic incompetence, namely, 9·3% of the total number of patients examined, was exceptionally high in comparison with an average incidence of 3·8% in eight other similar surveys reported in the literature. A large number of the patients with aortic incompetence had no symptoms of cardiovascular disease and had led active lives, remaining apparently well for many years. Of 201 patients with cardiovascular syphilis tested serologically, 189 (94%) had strongly positive serological reactions at the time of diagnosis, 4 (2%) gave doubtfully positive reactions, and in 8 (4%) the serological reactions were repeatedly negative. Of 27 cases which came to necropsy the diagnosis of cardiovascular syphilis was confirmed in all but one instance. In 214 cases in the series there was evidence of cardiovascular disease which was considered to be non-syphilitic.

A. J. King

597. **Outcome of Uncomplicated Syphilitic Aortitis**
R. E. IRVINE. *British Medical Journal* [*Brit. med. J.*] 1, 832–834, April 14, 1956. 2 figs., 12 refs.

Among 1,330 patients suffering from syphilis [see Abstract 596] who were investigated for evidence of cardiovascular disease, clinically, by cardioscopy, and by electrocardiography, 61 were thought to be suffering from uncomplicated syphilitic aortitis, 37 of them being men and 24 women, their ages ranging from 36 to 73 (average 56) years. In 24 cases, all in men, the probable duration of the infection was known, and varied from 13 to 37 years, with an average of 27 years; 10 of the patients had had some treatment at an early stage of infection, but only 2 had received more than one course of treatment with arsenicals.

The diagnosis was based on fluoroscopic evidence of dilatation of the aorta, observed on more than one occasion and in the absence of aortic incompetence. Hypertensive patients were excluded unless there was calcification of the ascending aorta (2 cases) or unless the patient subsequently developed aortic incompetence, in which case the diagnosis was made retrospectively (2 cases). In 47 cases the patient was free from symptoms; the remaining 14 patients had symptoms such as breathlessness or pain in the chest which may or may not have been due to aortic disease. At the time of the latest assessment (1954) 51 of the patients were still alive and 10 had died; the period of observation varied from 3 to 14 years (average 5·1 years). There appeared to be no significant difference between the survival rate of these patients and that of the general population of the same age and sex. During observation there was evidence of progression in 18 cases (30%), 15 patients developing evidence of aortic incompetence and 2 showing evidence of increased aortic dilatation; the remaining patient was thought to have an aortic diastolic murmur which, however, subsequently disappeared. In only 5 of these cases was the evidence of progression accompanied by increase in disability, namely, breathlessness in 3 cases and angina of effort in 2.

The electrocardiogram was normal in all the cases initially, but in 6 of the 18 cases showing progression the tracing later became abnormal. The pattern of left ventricular strain appeared in 3 of the cases in which aortic incompetence developed, and in 2 others with earlier symptoms of angina there was evidence of cardiac infarction, while in one case right bundle-branch block developed. The average interval before progression was detected was 3·4 years after diagnosis. In only one case was death due to cardiovascular syphilis, the patient having developed aortic incompetence. The remaining 9 died from other causes. There was some evidence to suggest that those with symptoms at the time of diagnosis and those with a greater degree of aortic dilatation fared more badly than the others. There was no evidence that age, sex, occupation, duration of infection, the presence of various physical signs, or the amount of treatment given after diagnosis had any appreciable effect on the liability to progression. Progression appeared to occur in an abnormally high proportion of cases in this series, the incidence of progression in five similar reported series ranging from 6·5 to 19·1%.

A. J. King

598. **The Use of the Nelson–Mayer Treponemal Immobilization Test in Serologically Latent Syphilis.** (Utilisation du test d'immobilisation des tréponèmes de Nelson–Mayer dans le domaine de la syphilis sérologique latente)
J. THIVOLET and M. ROLLAND. *Presse médicale* [*Presse méd.*] 64, 497–498, March 17, 1956. 7 figs.

Writing from the Faculty of Medicine, Lyons, the authors state that the majority of new cases of syphilis are at present diagnosed in the latent stage, and cite a number of reports in support of this contention. The serological tests therefore assume an even greater importance than before, and the treponemal immobilization (T.P.I.) test has proved to be one of the most reliable.

They then report the results obtained with standard tests for syphilis performed on 424 patients, various serological tests being carried out on each specimen of serum. These indicated that 279 of the patients

had latent syphilis, while 145 gave biological false positive reactions. When the T.P.I. test was performed on the sera of these patients the result was positive in 249 (89·3%) of the 279 cases of probable latent syphilis and negative in 30 cases (10·7%). Of the 145 cases of presumed false positive reactions the T.P.I. reaction was negative in 110 (75·9%) and positive in 35 (24·1%). Thus, assuming that the T.P.I. test is both very specific and highly reproducible, its systematic use prevented diagnostic error in 65 out of the 424 cases, 30 patients thought to have latent syphilis being shown to be biological false positive reactors, while 35 patients thought to be non-syphilitic were shown to have the disease. Results are given of the various standard serological tests employed, and the possible aetiology of the 145 biological false positive reactions is considered.

The authors then discuss the use of the quantitative T.P.I. test and claim that this test, performed at regular intervals during the follow-up period, provides the best guide to the efficacy of antisyphilitic treatment in latent syphilis. Finally they describe studies in which the quantitative T.P.I. test and an intradermal reaction with a preparation of dead treponemes was used in an attempt to assess the duration of the syphilitic infection in cases of latent syphilis. *R. D. Catterall*

599. **The *Treponema pallidum* Immobilization Test: a Diagnostic Aid to the Clinician**
R. K. LEDBETTER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1392–1393, April 21, 1956. 11 refs.

600. **The Place of the Reiter Cultivable Treponeme in the Serology of Syphilis.** (La place du tréponème de culture souche Reiter dans la sérologie de la syphilis)
P. GASTINEL, A. VAISMAN, and A. HAMELIN. *Annales de l'Institut Pasteur* [*Ann. Inst. Pasteur*] **90**, 249–257, March, 1956. 1 fig., 32 refs.

The Reiter cultivable treponeme was grown at the Institut Alfred Fournier, Paris, in Brewer's medium or glucose broth enriched with 10% of serum. After a week the organisms were harvested, washed in saline, and finally re-suspended in 0·3% phenol–saline. This suspension was used undiluted or at a low dilution as the antigen in a cold complement-fixation technique of the Kolmer type. As it was anticomplementary, great care was needed in the adjustment of the haemolytic system. In a series of tests carried out in parallel the results obtained with the above preparation, with Gaehtgens's "palligen", and with the Italian preparation "pallignost" were identical.

The treponemal immobilization (T.P.I.) test, the Wassermann reaction (W.R.), and the Reiter complement-fixation (C.F.) test were carried out in parallel on 511 sera, with 410 of which the three tests gave concordant results. With 25 sera the T.P.I. reaction was positive and the Reiter C.F. reaction negative, whereas with 48 the T.P.I. reaction was positive and the W.R. negative. Taking the T.P.I. test as a yardstick, this suggests that the Reiter C.F. test is more sensitive than the W.R. With 14 sera (2·7%) the Reiter C.F. reaction was positive but the result of the T.P.I. test was negative; in contrast, 34 sera (6·65%) gave a positive W.R. and a negative T.P.I. reaction. On this basis it is concluded that the Reiter C.F. test is of definitely higher specificity than the W.R. [No clinical details are given regarding the source of the sera tested.]

When rabbits and mice were inoculated with the Reiter treponeme there was a rise in titre in the W.R. and the Reiter C.F. reaction, but the animals did not develop immobilizing antibody. When the Nichols strain was used for inoculation, however, all three reactions became positive. *A. E. Wilkinson*

601. **Influence of the Wassermann Test on Pregnancy and Childbirth**
C. C. DENNIE. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 472–475, May, 1956. 1 ref.

602. **Massive-dose Arsenotherapy of Early Syphilis by Intravenous "Drip" Method. Five-day Treatment**
L. CHARGIN and W. LEIFER. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 482–484, May, 1956.

GONORRHOEA

603. **Treatment of Acute Gonococcal Urethritis in the Male with Single Dosage of Intramuscular Oxytetracycline**
E. BRAFF, W. DAVID, H. PERKINS, R. KOCH, G. GARA, and W. STEPHENS. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 110–112, Feb., 1956. 5 refs.

At the San Francisco City Clinic the authors have found an increasing number of patients to be intolerant of penicillin, and especially of those preparations in delayed adsorption vehicles which have become "the essential cornerstone of therapy" for gonorrhoea and syphilis. Oxytetracycline given by mouth has been shown to be effective against gonorrhoea, but this has involved the taking of regular doses over a variable period of days, whereas "the ideal medicament is one that can be given in one dosage under supervision". With the advent of injectable oxytetracycline, therefore, a study of the treatment of acute gonorrhoea with this preparation in a single dose of 400 mg. (given in two separate intramuscular injections) was carried out on 135 male patients. Prostatic or urinary cultures made approximately one and 2 weeks after treatment were negative on both occasions in 70 cases, in 27 cases a single culture only was made and was negative, and in 10 cases failure of treatment was presumed in that a positive culture was obtained after one or 2 weeks, though some of these may have been due to reinfection. The remaining 28 patients failed to return. The cure rate for cases in which two cultures were made after treatment was thus 87·5%, and if the cases in which only one culture was made were included the rate was 90·7%. These compare favourably with the results obtained with other injectable antibiotics. The only side-effect of oxytetracycline noted was "burning" at the time and site of injection. *Douglas J. Campbell*

Tropical Medicine

604. **Mycetoma in the Sudan**
P. ABBOTT. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. roy. Soc. trop. Med. Hyg.*] **50**, 11–24, Jan., 1956. 11 figs., 30 refs.

In certain parts of the world mycetoma is a serious and common disease resulting in much mutilation. In the Sudan, in a 2½-year period, 1,231 cases were admitted to hospitals and many more seen in out-patient departments, the incidence being highest in the central belt, between latitudes 12° and 20° North, and closely correlated with the rainfall.

In a series of 207 cases (172 in males and 35 in females) seen at Wad Medani Hospital between January, 1952, and June, 1954, there were 213 tumours, 168 on the foot, 19 on the leg, 14 on the hand, and 12 on other parts of the body. These included 4 cases of intraosseous and 5 of periosteal tumour, the author suggesting that in the former type the infection may be blood-borne, possibly from spores inoculated directly into a vein by the prick of a thorn. The clinical course, pathology, and epidemiology of the disease are described and discussed with reference to this series, and the author gives his reasons for regarding *Glenospora khartoumensis* as identical with *Madurella mycetomi*.

In the hope that it may be possible with chemotherapy in future to avoid the necessity for amputation in advanced cases the author tested the activity of some of the newer antibiotics against *M. mycetomi* and *Nocardia somaliensis in vitro*. The growth of *M. mycetomi* was unaffected by chloramphenicol, oxytetracycline, carbomycin, and polymyxin B. *N. somaliensis* on the other hand was markedly sensitive to all these antibiotics except polymyxin B, and was inhibited by carbomycin in a concentration as low as 1 μg. per ml. Clinical trials on an adequate scale proved impossible to arrange owing to the difficulty of following up most patients, but a number of patients infected with *N. somaliensis* who were given long courses of treatment with oxytetracycline and carbomycin showed a good response, with closure of sinuses and diminution in the size of the mass. In one case of infection of the foot involving the metatarsal bones which was followed up for 2 years repeated courses of antibiotics were given over a period of 9 months, when the condition appeared to be cured, but 13 months later a sinus reopened and discharged grains; further treatment led to cessation of activity.

As expected, cases of black mycetoma, due to infection with *M. mycetomi*, were unaffected by antibiotics. However, the organism was tested with five members of the aromatic diamidine series *in vitro*, and was found to be partially sensitive to all and markedly sensitive to one of them, diamidinodiphenylamine dihydrochloride, which at *p*H 7·0 inhibited the growth of 4 strains of *M. mycetomi* in a concentration of less than 3 μg. per ml. Intra-arterial injections of 25 to 50 mg. of this drug, given slowly, were well tolerated by human volunteers, but 9 patients who were given injections of the drug into the femoral artery twice weekly for 5 weeks showed no improvement. In spite of these failures the author considers this drug to be worthy of further investigation, and suggests giving it by infiltration into the lesion, possibly with the addition of hyaluronidase.

C. L. Pasricha

605. **The Problem of False Positive Reactions for Syphilis in Leprosy.** (Le problème des fausses réactions syphilitiques dans la lèpre)
L. LAURET and P. KERBASTARD. *Bulletin de la Société de pathologie exotique et de ses filiales* [*Bull. Soc. Path. exot.*] **48**, 789–795, 1955. 10 refs.

Being somewhat sceptical of the statement that the frequent finding in patients with leprosy of positive reactions to the usual serological tests for syphilis (S.T.S.) is due to the leprosy, the authors, working at Bamako in French Sudan, carried out a series of tests on treated and untreated lepers and on non-leprous subjects. The tests employed were the treponemal immobilization (T.P.I.) test of Nelson, and the Kolmer, Kline, and V.D.R.L. tests with the antigens of the Pasteur Institute.

Positive S.T.S. reactions were obtained in 34% of 126 apparently healthy African subjects and in 31% of 239 African lepers who had been treated with sulphones for a considerable time; treatment of the latter group with 2·4 mega units of penicillin produced a fall in titre of the positive reactions in the majority. Examination of 142 untreated lepers gave a positive S.T.S. reaction in 42%; in this group the tests used gave results in close accordance with the T.P.I. test. The authors believe that the positive S.T.S. reactions in all these cases can be attributed to endemic syphilis or other latent treponematosis, and conclude that their results do not support the commonly accepted statement that leprosy may be responsible for false positive S.T.S. reactions.

Robert Lees

606. **Bone Changes in Tropical Ulcer**
J. S. BROWN and J. H. MIDDLEMISS. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 213–217, April, 1956. 19 figs., 4 refs.

Tropical ulcer is a chronic condition seen in many parts of Africa, and occurs almost exclusively below the knee. Trauma and infection are probably the main aetiological factors, Vincent's organs often predominating. The present authors have studied cases from East, Central, and West Africa and present a detailed account of the *x*-ray changes which may occur.

The earliest visible change is a fusiform periosteal reaction in the tibia under the ulcer, which may be quite extensive. "Onion peel layering" or radiating spicules may occur, and the new bone may show a saucer-shaped area of destruction centrally, with or without sequestration. Continuing ulceration may produce a very thick deposition of new bone, like an ivory osteoma. Some-

times the original cortex is absorbed and the bony swelling contains cancellous bone. There may be remote changes, particularly in the fibula, with irregular widening and bony spicules projecting from the surface. Deformities are frequently found, alteration of the line of the ankle joint and tibial bowing being the most common. In long-standing cases epitheliomatous change may occur in the ulcer, the underlying bone being invaded and destroyed, causing a deeper and more irregular gap than that resulting from cortical sequestration. *D. E. Fletcher*

607. **Sickling in Relation to Morbidity from Malaria and Other Diseases**
A. B. RAPER. *British Medical Journal* [*Brit. med. J.*] 1, 965–966, April 28, 1956. 4 refs.

Over a period of approximately one year the blood of all children admitted to the Mulago Hospital, Kampala, Uganda, was tested for sickling. Among 818 children so tested, 130 were found to be heterozygous for the sickling gene (31 patients admitted with sickle-cell anaemia being excluded). Among children suffering from pneumonia, upper respiratory infections, diarrhoea and vomiting, poliomyelitis, tuberculosis, meningitis, and malnutrition the average proportion of "non-sicklers" to "sicklers" was 5·3 : 1. Among 30 patients with hookworm infection, however, the ratio was 14 : 1, and the author suggests that although this finding might be due to chance, it merits further investigation. Among 136 cases of malaria (*Plasmodium falciparum*) the ratio was 9·5 : 1 and of the 47 cases of cerebral malaria and 6 cases of blackwater fever, all occurred in "non-sickling" children. The death rates in hospital from all diseases, including malaria, for "sicklers" and "non-sicklers" did not differ very materially. But the higher incidence of severe forms of malaria among the latter shows that without treatment they would be at a disadvantage.

These results tend to confirm the views of other workers that although children heterozygous for the sickling gene may occasionally die from malaria, they are less likely to do so than children with a normal blood picture. *R. R. Willcox*

608. **Sickling and Malaria in the Gold Coast**
M. J. COLBOURNE and G. M. EDINGTON. *British Medical Journal* [*Brit. med. J.*] 1, 784–786, April 7, 1956. 16 refs.

The suggestion that the sickle-cell trait protects the bearer from the effects of malaria in hyperendemic malarial areas has never been definitely confirmed. As a further contribution to this topic the authors describe studies carried out at the Medical Research Institute, Accra, Gold Coast. The rapid metabisulphite method was used to detect the presence of the sickle-cell trait, and the malaria parasite density was calculated from thick films in relation to 400 leucocytes, on the assumption that the leucocyte count was 8,000 per c.mm.

Examination weekly of the blood of 46 babies in Accra showed that at the end of 6 months 6 out of 11 "sicklers" and 22 of 35 "non-sicklers" had contracted malaria; the difference is only slightly significant. Later, 1,015 inhabitants of Accra and 680 Frafras from the Northern Territories of the Gold Coast were examined for comparison of the parasite rate and density with the presence or absence of the sickle-cell trait. Again the figures (which are tabulated by areas) show no very significant differences, but whereas in Accra the trait appeared partially to protect the bearer against *Plasmodium falciparum* infection in all age groups, no evidence of such protection in the northern villagers over the age of one year was found. It is suggested that differences in the intensity of malaria transmission and in the incidence of haemoglobin C between the two areas may account for these findings.

[No information is given about the possibility of the influence of antimalarial drugs in either group, or of the weaning and dietetic habits; nevertheless, this is a stimulating if inconclusive paper. No answer is given here to the question whether in hyperendemic malarial regions it is safer to be a sickly suckling or a suckling sickler.] *Clement C. Chesterman*

609. **Treatment of Amebic Liver Abscess with Oral and Intravenous Administration of Aureomycin and Terramycin**
E. H. SADUN, V. VIRANUVATTI, and T. HARINASUTA. *Gastroenterology* [*Gastroenterology*] 30, 257–269, Feb., 1956. 7 figs., 20 refs.

At Siriraj Hospital (University of Medical Sciences), Bangkok, 17 adult patients with amoebic abscess of the liver were treated with aureomycin or oxytetracycline. Six patients received aureomycin by mouth in a total dosage of 14 to 28 g., the daily dose starting at 2 to 4 g. and then diminishing. The contents of the abscess were removed by aspiration where possible. In 3 cases there was no response; in the other 3 there was a good initial response, but 2 subsequently relapsed. Aureomycin was given intravenously in a total dosage of 10 g. (0·5 g. every 12 hours for 10 days) to 7 patients, 3 of whom also received 20 g. of aureomycin by mouth. The results of this treatment were good in 5 cases, there was no response in one, and one patient died. Oxytetracycline was given intravenously (0·5 g. every 12 hours) in a total dosage of 7 to 10 g. to 4 patients. The results were good in 3 cases (one of which relapsed later) and there was no effect in the fourth. The 8 patients who failed to respond to these treatments or who relapsed were treated with chloroquine by mouth or with emetine intramuscularly and good results were obtained. [Full reports of many of these cases are given, for which the original paper should be consulted.]

It is concluded that aureomycin by mouth is unsatisfactory in the treatment of amoebic liver abscess, and that although intravenous aureomycin and oxytetracycline produced rather better responses, they are still inferior to chloroquine and to emetine. Although the antibiotics were given in high dilution by intravenous drip infusion, thrombophlebitis occurred very frequently. Otherwise there were no toxic effects. The further study of the treatment of amoebic liver abscess with these drugs is recommended. *F. Hawking*

Allergy

610. **Prednisone and Prednisolone in the Treatment of Allergic Diseases**
L. H. CRIEP. *Journal of Allergy* [*J. Allergy*] **27**, 220–230, May, 1956. 8 refs.

To evaluate the anti-allergic potency of prednisone and prednisolone 96 patients with active allergic manifestations were treated with these two drugs at the Montefiore Hospital, Pittsburgh. Among the patients were 33 with bronchial asthma, 23 with perennial or seasonal allergic rhinitis, and 40 with atopic dermatitis, urticaria, or contact dermatitis. About two-thirds of them received prednisolone and the remainder prednisone. The starting dosage was 30 to 60 mg. a day, which after 3 to 6 days was gradually tapered off to a maintenance dose of 5 to 10 mg. daily. The period of treatment did not exceed 4 months. The symptomatic improvement was almost universally satisfactory; there was no instance of raised blood pressure, peripheral oedema, or hypopotassaemia. Abdominal pains occurred in 4 cases, in 2 of which they were relieved with aluminium hydroxide. " Moon face " was observed in 3 cases.

The author concludes that prednisone and prednisolone are very effective corticosteroids, 3 to 5 times as effective as cortisone and 2 to 4 times as effective as hydrocortisone, though he does not consider their use to be a substitute for " adequate allergic diagnosis and allergic management ". *H. Herxheimer*

611. **Prednisone in Allergic Diseases**
A. R. FEINBERG and S. M. FEINBERG. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 264–266, Jan. 28, 1956. 8 refs.

In a study carried out at the Northwestern University Medical School, Chicago, the effectiveness, potency, and side-effects of prednisone (the delta-1 analogue of cortisone) were compared with those of cortisone in the treatment of 80 patients with allergic diseases. The total 24-hour dose was divided into four 6-hourly doses for the first 2 days and three 8-hourly doses thereafter, the initial total daily dose being 20 to 30 mg. (that is, about one-fifth of that of cortisone), with subsequent maintenance doses reduced to 10 to 15 mg. per day.

Of 50 patients who had perennial chronic asthma, 41 obtained complete or nearly complete relief, and the symptoms of a further 10 patients with seasonal asthma related to pollen or mould allergy were well controlled. The majority of the 32 patients with seasonal allergic rhinitis responded well, a definitely poor result being obtained in only one. In 9 patients with atopic dermatitis, serum sickness, or chronic urticaria, the results were also good. (Many of the patients had more than one manifestation of allergy.) The side-effects included gastric complaints, increased appetite, excessive perspiration, urinary frequency, and muscle cramps, but none was serious. It seems that in allergic diseases prednisone is far less likely than cortisone to cause fluid retention, and there was no evidence of sodium retention. *G. B. West*

612. **The Treatment of Asthma with Prednisone.** (Le traitement de l'asthme par la prednisone)
P. VALLERY-RADOT, C. LAROCHE, and J. BONNET DE LA TOUR. *Presse médicale* [*Presse méd.*] **64**, 273–274, Feb. 15, 1956. 14 refs.

The authors report successful results in 16 cases of severe bronchial asthma treated with prednisone in an initial daily dosage of 25 to 60 mg. divided in 4 or 6 doses per day, later reduced in 13 cases to maintenance doses of 15 to 20 mg. per day. The results were better than or equal to those with cortisone and ACTH in the 12 who had previously received these hormones. The advantages of prednisone were the smaller dosage required and the notable absence of sodium retention. Some patients showed marked diuresis, but in spite of this, increase of weight occurred. In no case did hypertension or glycosuria develop, but in some there was a slight decrease in the plasma potassium level and the authors recommend the administration of potassium chloride; a Cushing-like syndrome was noted in a few cases. As with cortisone and ACTH, the remissions were of short duration, although in one case there was a complete remission which had lasted for 2 months at the time of the report. *Kate Maunsell*

613. **Continuous Steroid Hormone Treatment of Chronic Asthma. I. Cortisone and Hydrocortisone**
W. R. MACLAREN and D. E. FRANK. *Annals of Allergy* [*Ann. Allergy*] **14**, 183–193, March–April, 1956. 22 refs.

At Los Angeles County Hospital (University of Southern California) 52 patients, most of whom were suffering from severe chronic asthma, were treated with cortisone or hydrocortisone in initially high doses (100 to 300 mg. per day) which, after 1 to 2 weeks, were reduced to maintenance levels of 50 to 100 mg. per day for cortisone, and 20 to 60 mg. per day for hydrocortisone.

In 36 cases the results were assessed as " excellent " or " good ", in 13 as " fair ", and in 3 as " poor ". The patients were maintained satisfactorily for periods up to 28 months, and no serious complications occurred. In one patient a small duodenal ulcer, which was discovered after 2 months of treatment, was treated successfully by diet. In another patient an old osteomyelitis of the hip was reactivated, but responded to the administration of streptomycin; in both these cases steroid treatment was not interrupted. In most of the cases desensitization measures and the patient's customary palliative medication were continued during the hormone therapy. *H. Herxheimer*

Nutrition and Metabolism

614. **Aminoaciduria in Rickets and Tetany in Children.** (L'amino-acidurie du rachitisme commun et de la tétanie du nourrisson)
P. ROYER, A. SPAHR, and S. BERBEAUX. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 254–258, Jan. 22, 1956. 4 figs., 9 refs.

In a study carried out at the Clinique Médicale des Enfants, Paris, the amino-acid content of the urine of 44 children with rickets due to vitamin deficiency and of 7 infants with hypocalcaemic tetany was estimated by means of paper chromatography, and showed a general increase in 41 of the former and 4 of the latter. In particular, increased quantities of serine, glycine, threonine, histidine, and glutamic acid were present. When vitamin D_2 (calciferol) or D_3 was given the abnormal amino-aciduria disappeared, but it was unaffected by treatment with dihydrotachysterol ("A.T.10"). The authors conclude that the amino-aciduria was related more or less directly to the vitamin-D deficiency.

It is pointed out that in view of these findings the presence of increased amounts of amino-acids in the urine of patients with rickets does not necessarily mean that they are suffering from Fanconi's syndrome or allied disorders. *G. A. Smart*

615. **Studies on the Effect of Ethylenediaminetetraacetic Acid in Hypercalcemia**
H. SPENCER, J. GREENBERG, E. BERGER, M. PERRONE, and D. LASZLO. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 29–41, Jan., 1956. 3 figs., 11 refs.

Infusions of the chelating agent sodium ethylenediaminetetraacetic acid (Na-EDTA) were given to 8 patients at Montefiore Hospital, New York, with hypercalcaemia in the hope of preventing irreversible renal damage. In every case there was a temporary lowering of the serum level of the oxalate-precipitable calcium, which, however, did not fall below the normal except in one instance. There was no rise in the total serum calcium value. These findings contrasted with those in healthy controls; in the latter there were minor fluctuations only in the serum level of the oxalate-precipitable calcium while the total serum calcium level rose steeply. The authors suggest that a compensatory replenishment of the serum calcium from body stores occurs only if the level of the oxalate-precipitable fraction is reduced below the normal.

The 24-hour urinary excretion of calcium rose in every case above the pre-infusion level, but the rise was considerably lower in the hypercalcaemic patients than in controls. The authors point out that if the assumption is correct that in these patients replenishment of serum calcium from body stores does not occur, then excess calciuria should not be observed. They suggest two possible explanations for this anomaly: (1) there was a short period of hypocalcaemia which was not detected in the blood samples analysed; or (2) any lowering of the serum level of the oxalate-precipitable calcium, even if it is not reduced below normal limits, may result in a small compensatory drain of calcium from body stores.

Side-reactions were few and insignificant. In most of the patients slight hypotension was observed, while in one patient there was transient albuminuria and in another oliguria. Hypocalcaemic tetany occurred once and responded rapidly to intravenous administration of calcium gluconate. Damage to tubular epithelium was found at necropsy in one case, but it is doubtful whether this could be attributed to the chelating agent. Clinical improvement was obtained in only one case. Since the changes in the blood chemistry were temporary the authors recommend infusions of Na-EDTA only to tide the patient over until more radical treatment can be given. *R. Schneider*

616. **Studies on Agammaglobulinemia. VI. Hemostasis in Patients with Agammaglobulinemia**
P. G. FRICK and R. A. GOOD. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **91**, 169–172, Jan., 1956. 14 refs.

The authors, working at the University of Minnesota, Minneapolis, have studied the activity of the various blood clotting factors in 7 patients (6 male and 1 female) with complete agammaglobulinaemia. The congenital form of agammaglobulinaemia was present in 4 patients, all children, and the acquired type in 3 adults. The factors studied included the bleeding, clotting, prothrombin, thrombin, and recalcification times, the concentration of labile and stable prothrombin conversion factors, prothrombin, and fibrinogen, the platelet count, capillary fragility, and fibrinolysis.

No abnormality in plasma clotting factors was observed, but in 5 of the 7 cases, including all 4 of congenital agammaglobulinaemia, the platelet count was raised, the values being 256,000 to 558,000 per c.mm. (normal 150,000 to 220,000 per c.mm.). The authors consider that their findings support the following conclusions: (1) none of the protein factors concerned with blood coagulation is a gamma globulin; (2) agammaglobulinaemia is probably the result of an isolated deficiency of a single enzyme system in protein synthesis; and (3) since other protein factors were found to be normal it is likely that gamma globulin is not formed in the liver.
D. G. Adamson

617. **Idiopathic Paroxysmal Myglobinuria. Report of Two Cases and Evaluation of the Syndrome**
L. REINER, N. KONIKOFF, M. D. ALTSCHULE, G. J. DAMMIN, and J. P. MERRILL. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 537–550, May, 1956. 11 figs., 28 refs.

Gastroenterology

PHARYNX AND OESOPHAGUS

618. **Management of Pharyngostome, Esophagostome and Associated Fistulae**

J. J. CONLEY. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol.* (*St Louis*)] **65**, 76–91, March, 1956. 10 figs.

In this paper from St. Vincent's Hospital, New York, the causes of fistula formation after an extensive operation on the neck are stated to be infection, failure of stitches, poor tissues (usually due to previous irradiation), and lack of support in the wound. The most common type of fistula is that which follows total laryngectomy; this is usually small, and closes spontaneously if given time. So may also the fistula which develops after pharyngo-laryngectomy, though it is often larger and needs surgical repair. Fistulae occurring after radical excision of the tongue or after a block dissection of the neck are usually large and almost always require reconstructive surgery. The formation of a fistula following an attempt to reconstruct the pharynx after excision of a carcinoma is uncommon. For the repair of large fistulae which occur after combined surgery and radiotherapy skin flaps from the neck or chest may be needed. The author outlines the operations which may be complicated by fistula formation and discusses measures aimed at its prevention. *William McKenzie*

619. **Haematemesis Controlled by Adrenaline and Stypven**

W. J. M. BRANDON. *Lancet* [*Lancet*] **1**, 360–362, April 7, 1956. 3 refs.

In this article from Law Hospital, Carluke, Lanarkshire, the author describes a method of treatment of recurrent haematemesis from peptic ulcer with adrenaline and Russell's viper venom (" stypven ") applied locally. The treatment is given only to patients who have had a second haematemesis while under routine medical treatment in hospital. When this occurs a stomach tube is passed and the stomach washed out with sterile water, after which 20 ml. of adrenaline hydrochloride solution (1 in 1,000) is inserted down the tube, which is left *in situ*. After 20 to 30 minutes the process is repeated and this time the adrenaline is followed by 5 ml. of stypven and 5 ml. of sterile water. (The purpose of the adrenaline is to produce temporary ischaemia, enabling the stypven to form an occlusive clot without being washed away.) The tube is then withdrawn and a slow transfusion of 2 to 4 pints (1·1 to 2·3 litres) of blood is started. The medical dietary regimen is resumed the next day. Emergency gastrectomy is performed only if haemorrhage recurs again within 72 hours of this treatment, which may, if necessary, be repeated before operation. Otherwise the decision whether to operate or not may be deferred until the patient has recovered sufficiently for a barium-meal examination to be carried out. It is stated that since this method was adopted the mortality in cases of haematemesis has fallen from about 12 to 7·6%, the annual number of cases treated ranging from 68 to 93.

[This article is largely in the form of a description of the stages of development of the technique and the reasoning which led up to them. Only the barest numerical details are given, and the improvement in mortality reported is based on the results for one year only. However, the author claims only to have shown that " the method is worthy of a more extended trial ".] *J. Warwick Buckler*

LIVER

620. **The Metabolism of Water and Electrolytes in Patients with Cirrhosis of the Liver**

P. J. TALSO, I. H. STRUB, and J. B. KIRSNER. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 210–226, Feb., 1956. 3 figs., 35 refs.

The nature of the defect in electrolyte and water metabolism in cirrhosis of the liver was studied at the University of Chicago by metabolic balance studies and by determining the distribution of water and electrolytes in muscle biopsy specimens from one healthy subject and 4 patients suffering from cirrhosis with ascites and peripheral oedema. The patients were maintained on a constant dietary intake of protein, fat, and carbohydrate, with a sodium intake of 25 or 50 mEq. daily. They also received, during some periods of the investigation, an ion-exchange resin by mouth and mercurial diuretics by subcutaneous injection.

The over-all weight loss of the 4 patients with cirrhosis was 10 to 18 kg., with a cumulative negative sodium balance of 430 to 1,800 mEq. In 3 of the patients there was a cumulative negative potassium balance. Analysis of muscle biopsy specimens from the cirrhotic patients showed a large increase in the volume of extracellular fluid, while the volume of intracellular fluid was normal in the deltoid muscle and slightly decreased in the gastrocnemius muscle. After diuresis and disappearance of obvious oedema there was still a significant increase in the volume of extracellular fluid. No significant change was observed in the intracellular concentrations of sodium or potassium before or after treatment. The authors conclude that their studies " provide evidence . . . that the oedema and ascites in cirrhosis of the liver represent an isotonic expansion of the extracellular phase ".

[The data derived from examination of muscle biopsy specimens from the cirrhotic patients clearly show that the increase in tissue fluid is confined to the extracellular phase, but the conclusion that this expansion is isotonic is not supported by the figures given. The serum sodium level in the one cirrhotic patient for whom complete information is given was 132 mEq. per litre initially,

rising to 148 mEq. after diuresis, while 2 other patients are said to have developed hyponatremia during the course of the investigation.] *E. Keith Westlake*

621. **Treatment of Bleeding from Portal Hypertension in Patients with Cirrhosis of the Liver**
C. S. WELCH, J. E. KILEY, T. S. REEVE, E. O. GOODRICH, and H. F. WELCH. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 493–502, March 15, 1956. 3 figs., 39 refs.

This paper deals with the problem of haemorrhage, especially from dilated oesophageal veins, in cases of portal hypertension due to hepatic cirrhosis. The authors first point out the great difference in prognosis between bleeding from a peptic ulcer and from oesophageal veins, due mainly to the profound and unpredictable effects of the associated dysfunction of the liver in the latter. In a few cases of portal hypertension (approximately 10%) the cause is extrahepatic and there is no liver disease, but even in these the prognosis after haemorrhage is bad.

Out of 50 consecutive cases of portal cirrhosis and massive haemorrhage admitted to the Albany Medical Center, Albany, New York, between 1946 and 1953, 33 (66%) were fatal. Of those patients suffering a first haemorrhage, 76% died. Coma preceded death in 39% of cases, and the possible causes of the coma, especially in relation to the bleeding, are fully discussed but without any conclusions being reached.

For the immediate treatment of haemorrhage from the oesophageal veins the use of the Sengstaken–Blakemore oesophageal tampon is recommended; but although the haemorrhage can invariably be stopped with this tube, the over-all results obtained in this series in the 19 cases in which it was used are far from impressive, 13 patients having died, 9 of them in coma. For the subsequent treatment of survivors, the performance of a porta-caval shunt, after a careful study of the individual case, is advised and it is urged that the operation should be performed, if possible, before haemorrhage occurs. The mechanism of coma and the possibility of its prevention are discussed, but these problems are clearly still unsolved. *J. W. McNee*

622. **Liver Changes in Alcoholic Polyneuritis.** (Polynévrites alcooliques et altérations hépatiques)
M. CACHIN, F. PERGOLA, R. LEVILLAIN, and F. JOUBAUD. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **72**, 61–68, Jan. 27, 1956. 8 refs.

Observations were made on 32 patients suffering from alcoholic polyneuritis, in all cases due to the consumption of red wine. The average age of the patients was 51 years (range 34 to 69). There was considerable variation in the symptoms, but in the majority there was both sensory and motor involvement. Treatment consisted in the gradual withdrawal of alcohol while giving a good diet supplemented with vitamins (especially vitamins B_1, B_{12}, C, and K), together with injections of liver extract. Six patients died, 3 from tuberculosis, 2 from cirrhosis, and one from general paralysis.

Cirrhosis, ascites, and a collateral circulation were present in 3 cases; in only 8 of the remainder was the liver definitely palpable. The results of flocculation tests, estimations of the serum protein and cholesterol concentrations and prothrombin time, and paper electrophoresis of the serum proteins performed on varying numbers of the patients were mostly inconstant, and in only 9 cases was definite evidence of a disturbance of liver function obtained. Needle biopsy of the liver was carried out in all cases and only in 2 did the liver appear normal. Fatty infiltration was present in all but 5 cases, and was usually marked. Fibrosis was also usually present, being severe in 10 cases, and infiltration by inflammatory cells was usually seen. Although there was some variation in the intensity of these changes from liver to liver, they appeared to be an integral part of the fully developed syndrome. In general, the intensity of the symptoms and of the hepatic changes were roughly parallel.
W. H. Horner Andrews

623. **Liver Changes in Delirium Tremens.** (Delirium tremens et altérations hépatiques)
F. PERGOLA, M. CACHIN, R. LEVILLAIN, and F. JOUBAUD. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **72**, 68–74, Jan. 27, 1956. 8 refs.

The authors have studied the condition of the liver in 33 cases of delirium tremens, 24 in men and 9 in women, usually due to the consumption of red wine. In 17 cases the precipitating factor was determined, being most commonly sudden deprivation of alcohol. Clinically, only 17 patients had hepatomegaly, while one had jaundice and other signs of liver failure and 2 had cirrhosis, ascites, and jaundice. Treatment consisted in vitamin therapy, intravenous injections of alcohol and strychnine and, when necessary, antibiotics. Five patients died, 3 as a direct result of their condition.

Hepatic function tests were performed on 29 patients, including various flocculation tests, paper electrophoresis of the serum proteins, and estimation of prothrombin time and serum cholesterol level (total and esterified). The authors conclude that 7 patients had frank hepatic insufficiency. The histology of the liver was examined in biopsy or necropsy specimens. In 5 cases the findings were normal, but treatment had been started before the specimens were taken. Fibrosis (28 cases) and fatty infiltration (26) were the commonest lesions, and in just under one-third they were well-developed. Inflammatory cellular infiltration (7 cases) and necrosis (4 cases) were also seen. The histological changes were considerably less in the fatal cases than in the others, and the authors emphasize that the prognosis in delirium tremens cannot be determined from the histological appearance of the liver. They consider that hepatic dysfunction plays no part in the pathogenesis of this condition. *W. H. Horner Andrews*

624. **Splenic Venography in Portal Cirrhosis of the Liver**
N. R. KONAR and D. C. R. CHAUDHURY. *American Journal of Gastroenterology* [*Amer. J. Gastroent.*] **25**, 363–379, April, 1956. 10 figs., 8 refs.

625. **Production of Impending Hepatic Coma by a Carbonic Anhydrase Inhibitor, Diamox**
L. T. WEBSTER and C. S. DAVIDSON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **91**, 27–31, Jan., 1956. 14 refs.

" Impending hepatic coma " here refers to confusion, with or without a " flapping " tremor, developing in the presence of severe hepatic disease. In an investigation made at the Boston City Hospital acetazolamide (" diamox ") was administered to 12 chronic alcoholics in whom cirrhosis was diagnosed clinically and by laboratory methods, confirmation being obtained by biopsy in 3 cases and at necropsy some months later in 2. In all cases fluid accumulation was present and sodium and protein intake were restricted. Diamox was given in a dosage ranging from 500 mg. on alternate days to 1 g. daily for 3 to 27 days. Patients were classified in two groups according to whether or not confusion (with or without tremor) developed. In the 4 patients placed in Group I confusion developed, in 3 of them with flapping tremor, within 2 to 48 hours of the first dose. Of the 8 patients who did not develop confusion (Group II), 3 became drowsy. There appeared to be no clinical difference between the two groups, but Group-I patients had previously had impending coma. Administration of potassium chloride did not affect the results. The level of blood ammonia nitrogen rose about equally in both groups. The nitrogen contained in the diamox did not appear to be the direct cause of the rise in blood nitrogen content, and a possible effect of diamox on brain metabolism is postulated.

W. H. Horner Andrews

PANCREAS

626. **Fibrocystic Disease of the Pancreas, a Generalized Disease of Exocrine Glands**
P. A. DI SANT' AGNESE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 846–853, March 10, 1956. 1 fig., 14 refs.

Fibrocystic disease of the pancreas is a hereditary condition affecting many, perhaps all, of the exocrine glands, with clinical manifestations in the pancreas, lungs, liver, sweat glands, and salivary glands. In children it accounts for almost all cases of pancreatic deficiency, most of those of chronic non-tuberculous pulmonary disease, and one-third of those of hepatic cirrhosis and portal hypertension. In hot weather abnormalities in the electrolyte content of the sweat may cause fatal massive salt depletion.

In the pancreas, eosinophil concretions in the ducts produce dilatation and parenchymal degeneration and fibrosis without diabetes mellitus; poor nutrition is accompanied by the classic features of pancreatic disease and the pathological manifestations of pancreatic achylia. In the respiratory tract, infections between the ages of a few months and 2 years are followed by bronchial dilatation and distension, repeated respiratory failure, blood infections, or diffuse atelectasis. Bronchial obstruction leads to a barrel chest, bronchitis, finger clubbing, and the *x*-ray appearances of emphysema and chronic bronchopneumonia, due usually to the haemolytic *Staphylococcus aureus*. Sudden asphyxia or acute cor pulmonale may terminate one of the bouts of acute infection. Focal biliary fibrosis is produced by concretions of eosinophilic material in the bile ducts and may progress to severe diffuse cirrhosis and portal hypertension, at which stage symptoms and abnormal pathological findings appear. The sweat glands secrete 2 to 4 times the normal amount of sodium, independent of any renal or adrenal dysfunction or steroid therapy. The volume and electrolyte content of the secretion of the salivary glands are abnormally high, but not diagnostically so. The duodenal contents may be abnormally viscous for obscure reasons not apparently related to any pancreatic or electrolyte disturbance so far identified. Meconium ileus may occur and may be accompanied by sterile peritonitis.

Diagnosis depends on the demonstration of complete absence of pancreatic secretion (of which excess fat in the stools on microscopical examination is satisfactory evidence, though duodenal intubation is desirable) with signs of pulmonary disease and high concentrations of chloride and sodium in the sweat. A history of the disease in siblings is useful, but not essential, and the presence of hepatic cirrhosis is an added clue. Prognosis depends mainly on the pulmonary disease, which runs its course usually in 2 or 3 years, though there may be considerable late clearing. Attention to treatment of the pancreatic insufficiency and to maintenance of general nutrition improves the prognosis, but there are always special hazards such as ileus, portal hypertension, and salt depletion in hot weather.

Out of 325 patients with this disease seen at the Babies Hospital, New York, over a period of 15 years, 145 are dead and 168 living, with 12 untraced. Of the survivors, 24 are now above the age of 10, and the oldest is 19 years old and well. To achieve these results a high-calorie diet (150 to 200 Calories per kg. body weight), with high protein (2 to 6 g. per kg.) and low fat content, a high content of simple sugars (glucose, cane sugar, banana), and a moderate starch content is given, together with 2,000 units of vitamin D and 10,000 units of vitamin A daily, pancreatic extract with each meal, and liberal salt—an additional 2 g. being given in hot weather. Penicillin and streptomycin have been given intramuscularly and by inhalation, and broad-spectrum antibiotics by mouth. While *x*-ray signs of pulmonary involvement exist, broad-spectrum antibiotics are given prophylactically. Bronchoscopy and chest surgery are rarely indicated, and abdominal surgery only for ileus or portal hypertension. Electrolyte therapy may become urgently necessary.

Recognition of the associated disturbances of the sweat and salivary glands has shown that the disease is not simply an abnormality of mucous secretion, but a widespread disorder of unknown basic nature. The name " mucoviscidosis " is thus incorrect, and although some such name as " generalized exocrinopathy " would appear to be more accurate, it is suggested that the term fibrocystic disease of the pancreas is best retained until the aetiology of the condition is clarified.

W. A. Bourne

Cardiovascular System

627. **A New Method for the Treatment of Congenital Heart Disease Associated with Impaired Pulmonary Circulation. An Experimental Study.** [In English]
F. ROBICSEK, A. TEMESVÁRI, and R. L. KÁDÁR. *Acta medica Scandinavica* [*Acta med. scand.*] **154**, 151–161, March 26, 1956. 5 figs., 23 refs.

This report from the Postgraduate Surgical Clinic, University of Budapest, describes the results of experimental operations performed on dogs with the aim of finding a procedure less complicated and with fewer disadvantages than the Blalock operation and other operative procedures for the relief of pulmonary stenosis. Details of the operation are given. It consists essentially in transection of the superior vena cava above the site of union with the azygos vein, followed by transection of the right pulmonary artery close to its origin from the main trunk, the peripheral stumps of the two vessels, whose walls are of equal thickness, being anastomosed end-to-end. The right lung is thus supplied with blood directly from the superior vena cava, the blood flow bypassing the heart. These experiments have shown that pulmonary blood flow is almost equal on the two sides, without any significant increase in blood pressure in the area of the superior vena cava. The operation has been performed on 15 dogs, of which 4 died as a result of the operation (one of empyema, one of bronchopneumonia, and 2 after obliteration of the anastomosis), but the remaining animals were able to move about and were eating well as early as 2 to 3 days after operation. At the end of 3 to 6 months they were subjected to detailed tests, when in 10 of the 11 survivors the anastomosis proved to be still functioning. Six months after the operation 5 of the animals were killed and at necropsy the veins of the superior vena caval system were found to be somewhat larger in diameter, the anastomosis was patent, and the suture line completely covered by endothelium; there were no pathological changes in the lungs.

The advantages claimed for this procedure over the Blalock operation and its modifications are: (1) it places no considerable extra burden on the heart; (2) it does not increase blood pressure in the main trunk of the pulmonary artery; (3) the anastomosis supplies " pure " venous blood to the lung; (4) endarteritis is not so liable to occur; and (5) it should not be technically difficult to perform, even on children. As regards adaptation of the operation to human patients, the authors point out that although at first glance it may appear too hazardous, the Blalock operation also at first appeared to be risky and complicated. They cite evidence to show that the human organism tolerates fairly well the obstruction of one vena cava, that the superior vena cava has previously been successfully anastomosed to the right auricle, and that a temporary clamping of one of the main branches of the pulmonary artery has been shown to produce no grave consequences even in a patient in poor condition.

D. P. McDonald

628. **The Treatment of Chronic Cor Pulmonale in Asthmatics with Adrenocortical Hormones (ACTH, Cortisone, and Cortisone Derivatives).** (Le cœur pulmonaire chronique des asthmatiques et son traitement par les hormones du cortex surrénal (ACTH, cortisone et dérivés))
J. TURIAF, P. BLANCHON, R. SAUVAN, and R. GEORGES. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] 72, 188–216, Feb. 24, 1956. 9 figs., 10 refs.

In this paper from the Hôpital Bichat, Paris, the authors report in great detail 4 cases of congestive cardiac failure complicating bronchial asthma which they treated successfully with adrenocortical hormones. All 4 patients were men, ranging in age from 41 to 62, with the classic history, physical signs, and radiographic appearances of asthma, which in one case had started in childhood and in the others in early adult life.

In the first case severe right-sided failure with cyanosis, orthopnoea, hepatosplenomegaly, massive oedema, and cardiac enlargement developed rapidly after a febrile illness resembling influenza which failed to respond to orthodox treatment with antibiotics, theophylline, digitalis, and mercurial diuretics. Six days after starting the administration of ACTH (corticotrophin) by intravenous drip infusion in a dose of 50 mg. daily there was a massive diuresis accompanied by clearing of the signs of cardiac failure, and on the 10th day the ACTH was discontinued. Several months later a further episode of right-sided failure was treated with hydrocortisone in doses gradually diminishing from 60 to 30 mg. daily, on which maintenance dose the patient was kept free from recurrence (and without complications attributable to adrenocorticoids) for a period of 16 months. The second patient had recovered from three previous episodes of right-sided insufficiency under orthodox treatment before he failed to respond during a fourth, which was associated with a spontaneous pneumothorax. Treatment with prednisone in doses diminishing from 40 to 15 mg. daily led to the disappearance of all signs of failure over a period of 2 to 3 weeks, but right bundle-branch block persisted. In the 2 remaining cases the right-sided failure was of a more chronic nature, but was again rapidly relieved by treatment with prednisone and a depot preparation of ACTH respectively, both patients being eventually stabilized on a maintenance dose of prednisone and a salt-free diet, with the addition of potassium chloride (1 g. daily) and biweekly injections of 50 mg. of testosterone.

In their discussion of these cases the authors point out the comparative rarity of right-sided cardiac failure as a complication of asthma, only 12 such cases having occurred in a series of 150 asthmatics, 11 of them in males. In a further 32 cases there was some evidence of pulmonary hypertension without insufficiency actually developing.

H. F. Reichenfeld

CHRONIC VALVULAR DISEASE

629. **Criteria for and Results of Surgery for Mitral Stenosis**

C. P. BAILEY and H. E. BOLTON. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **56**, 649–663 and 825–839, March 1 and 15, 1956. 21 figs., 41 refs.

The authors' experience at the Hahnemann Medical College and Hospital, Philadelphia, of valvotomy for mitral stenosis now covers 1,500 cases, 189 of which have been followed up for at least 5 years. They feel that the time has come to review the principles on which the technique of the operation and the selection of cases were originally based and to see whether any changes should be considered. The standard left-sided approach in which the valve was split by finger or guillotine knife achieved success with both commissures in only 47% of cases. More recently, in cases in which other valves might be involved, the authors have used a right-sided approach which also gives access to the tricuspid and aortic valves. This approach to the mitral valve also has the advantage that it allows the posterior commissure to be divided, producing a better opening, and avoids the areas of thrombosis which are present in 53% of patients with auricular fibrillation. The right-sided approach is achieved by enlarging the groove between the two atria posteriorly and controlling the opening made in the base of the groove with a purse-string suture.

The over-all operative mortality in the authors' first 1,000 cases was 7·7%; in good-risk cases it was as low as 3%, but reached 18% in bad-risk cases. Late deaths occurred in an additional 5·6%. Improvement is claimed in 89% of the survivors. A large heart constitutes a major risk, but a history of congestive failure or pulmonary oedema had little influence on the operative mortality. Auricular fibrillation developed after operation in 25% of cases, and only one-quarter of these reverted to sinus rhythm. Postoperative embolism occurred in 8·3% of cases, the majority of these already being in fibrillation. Only 9 patients out of 1,000 had to be explored again for presumed recurrence, but it is possible that in the course of years active disease may lead to re-stenosis or deterioration following an inadequate earlier operation in other cases.

T. Holmes Sellors

630. **Comparison between the Clinical Features and the Findings on Auricular Biopsy in 50 Cases of Mitral Disease Treated Surgically.** (Confrontation anatomo-clinique à partir de 50 biopsies auriculaires chez des mitraux opérés)

J. F. MARTIN, R. FROMENT, A. PERRIN, and J. BLANC. *Archives des maladies du cœur et des vaisseaux* [*Arch. Mal. Cœur*] **49**, 134–146, Feb., 1956. 5 figs., 23 refs.

In this paper from the Lyons Faculty of Medicine the authors describe the findings in auricular biopsy specimens taken at operation from 50 patients with mitral disease, between 15 and 60 sections being cut in each case, and relate them to the clinical course before and after operation. They distinguish three main types of lesion: (1) parenchymatous degenerative lesions, present in about half the cases, especially those with auricular fibrillation; (2) auricular thrombi, present in two-thirds of their cases, half being microscopic and half macroscopic; (3) Aschoff nodes, typical examples of which occurred in 20 of their 50 cases.

Out of 8 cases in which preoperative embolism occurred, microscopic auricular thrombi were found in 4 and macroscopic in one, whereas macroscopic thrombi were present in all 3 cases in which postoperative embolism occurred. Auricular thrombosis was present in 15 out of 17 cases of complete arrhythmia and in only 19 out of 33 cases with normal rhythm. Aschoff nodes, however, were rare in fibrillating hearts (3 out of 17 cases) compared with those in normal rhythm (17 out of 33 cases). From these findings the authors deduce that auricular fibrillation is a sign of haemodynamic disorder rather than of inflammatory activity.

Although the Aschoff node has always been regarded as an index of previous frank rheumatic activity, in this series the incidence of nodes was the same (approximately 50%) among patients with no history of joint manifestations as among those who had had frank arthritis. On the other hand rheumatic symptoms occurred 7 to 18 days after operation in 9 of the 20 patients with Aschoff nodes and in only 7 of the 30 without. Of the 20 patients in whom nodes were found at biopsy, only 3 had neither pre- nor post-operative manifestations of clinical rheumatic activity, whereas of the 30 in whom no nodes were found, 13 had no such manifestations. The authors therefore regard the Aschoff node as a sign of smouldering subclinical rheumatic activity and as a warning of a possible lighting-up of the inflammatory process by the trauma of surgical intervention.

J. Yell

CORONARY DISEASE AND MYOCARDIAL INFARCTION

631. **The Physiologic Explanation of the Changes in the Coronary Circulation following Prolonged Aortico-Coronary Sinus Anastomosis**

A. A. BAKST, R. MANIGLIA, and C. P. BAILEY. *Journal of Clinical Investigation* [*J. clin. Invest.*] **35**, 302–307, March, 1956. 2 figs., 6 refs.

Previous experiments on dogs, undertaken at the Hahnemann Medical College and Hospital, Philadelphia, to determine the results of Beck's operation for arterialization of the coronary sinus, showed that on ligation of the circumflex branch of the left coronary artery 1 to 2 months after operation the mortality was significantly reduced. The blood flow from the distal end of the cut artery was greater than in the normal animal, and a reduction in the oxygen saturation of this blood was interpreted as showing that it had passed in retrograde fashion through the myocardial capillaries as a result of the anastomosis between the aorta and the coronary sinus. Compression of this anastomosis diminished the reflux flow from the cut artery, but it remained higher than normal, which was taken to indicate that intercoronary arterial anastomotic channels had developed.

The authors now report similar observations made on two groups, each of 6 dogs, 6 and 12 months respectively after the operation. They found that the coronary sinus still carried arterial blood at high pressure, but that ligation of the circumflex coronary artery now had as high a mortality as in dogs which had not been operated on. The quantity of reflux blood flow from the divided artery was greater than in normal dogs, but was unaffected by temporary occlusion of the graft, while the blood was arterial in nature, implying that it had travelled by arterial anastomotic channels only. They conclude that in these animals the anastomosis between the aorta and the coronary sinus was no longer making any significant contribution to the myocardial blood supply in the form of retrograde flow, but that some intercoronary anastomotic channels appeared to have developed as a result of the operation. They draw attention to the gross intimal thickening which was present in the walls of the coronary sinus and its main venous tributaries in these animals and which was almost sufficient to occlude their lumen. *J. A. Cosh*

632. **The Electrocardiogram One Year after Acute Myocardial Infarction**
R. GITTLER, J. A. SCHACK, and H. VESELL. *American Heart Journal* [*Amer. Heart J.*] **51**, 246–260, Feb., 1956. 9 refs.

The electrocardiograms of 51 patients with acute myocardial infarction were analyzed at the time of their discharge from the hospital and again one year later. Behaviour of the QRS complex, the Q–T interval, the RS–T segment and the T wave is described. Serial changes noted in the electrocardiograms one year following myocardial infarction are reported.

In only one of 51 instances of acute myocardial infarction did the 12-lead electrocardiogram with typical changes return to normal one year later; a completely normal 12-lead electrocardiogram is therefore strong evidence against the presence of an acute myocardial infarction of the classical anterior or posterior wall type, one year previously.—[Authors' summary.]

633. **Simplified Heparin Therapy of Impending and Acute Myocardial Infarction**
H. ENGLEBERG. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 466–475, March, 1956. 1 fig., 38 refs.

Concentrated aqueous heparin (100 or 200 mg. per ml.) was given initially for 1 to 2 weeks before giving other anticoagulant drugs to a group of 19 patients in whom there were considered to be signs of impending myocardial infarction—that is, increasing angina and rapidly decreasing effort tolerance. The drug was injected subcutaneously in a dosage in most cases of 150 to 200 mg. every 12 hours, but in a few cases 300 to 400 mg. was given every 24 hours. After symptomatic improvement had been obtained standard anticoagulants were given by mouth, heparin being administered at the same time in a dosage of 200 mg. 2 or 3 times a week and continued for 2 or 3 months. Although the patients were ambulant, their activity was markedly restricted. In 2 of the patients transmural infarction and in 4 subendocardial infarction developed during treatment. No evidence of infarction was observed in 13 patients; 4 of these discontinued anticoagulant therapy after a short time, but 3 of them had an attack of myocardial infarction within 3 months of cessation of treatment. These results, in the light of others previously published, are considered to be good. Heparin was similarly given to 15 patients for the first 3 weeks following an acute attack of myocardial infarction [but the results are not reported]. This method of treatment is simple, reasonably cheap, and requires little laboratory control.

The author, discussing the properties of heparin other than that of preventing coagulation—for example, reducing alimentary lipaemia—considers that it is superior to and safer than prothrombin-depressing drugs. Haemorrhage due to heparin is usually mild and easily controlled. *J. N. Agate*

BLOOD VESSELS

634. **Intra-arterial Vasodilator Agents in the Treatment of Advanced Occlusive Arterial Disease of the Extremities. A Preliminary Report of a New Vasodilator Drug, 27 MI**
O. A. ROSE and A. EBEL. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **4**, 142–150 Feb., 1956. 10 refs.

The effects of a new vasodilator drug, 27 MI, described as the neutral thiophosphoric ester of 3-hydroxyphenyltrimethyl ammonium iodide trihydrate, were studied at the Veterans Administration Hospital, Bronx, New York. In 10 healthy controls intra-arterial injection of 27 MI resulted in maximum vasodilatation in the skin, but had little apparent effect on muscle blood flow. The drug was then given, also by intra-arterial injection, to 63 patients with advanced arterial occlusive disease of the lower limbs. It was well tolerated by the majority and did not give rise to any serious side-effects. There was relief of pain in 58, and healing of leg ulcers and necrosis was expedited. The dosage was 5 to 20 mg., the concentration of the solution being 10 mg. per ml. The frequency of administration varied according to the severity of the occlusive manifestations and the response obtained, and was usually reduced progressively. The injections, which were rarely continued for more than a month, were always given with the patient in the supine position. The average number of injections given to each patient was 20, but several patients received more than 50 into the same artery and one patient had more than 100.

Intra-arterial injection of vasodilator agents is considered to have the following advantages: (1) the effect is confined largely to the local vascular bed where it is most required; (2) it reduces to a minimum the diversion of blood into healthy vessels and away from those areas in which there is either evident or occult concomitant arterial insufficiency; and (3) side-effects are avoided or minimized.

It is concluded that 27 MI is a safe and effective vasodilator for administration by this route, and that the results of this investigation, together with previous

experience, indicate that this method of treatment is of particular value in patients with localized arterial occlusive disease, especially when there is concomitant vascular disease in other areas. *Leon Gillis*

635. **The Function and Structure of the Arteries as Related to Age. An Angio-chemical Study**
G. HEVELKE. *Angiology* [*Angiology*] 7, 39–54, Feb., 1956. 5 figs., 26 refs.

The relationship between function and chemical composition of the arteries was studied at Leipzig University, 10-cm. lengths of the brachial and femoral arteries from 96 subjects being examined post mortem. The arteries showed a progressive increase in weight with age, the brachial artery doubling in weight from the third to the eighth decade while the weight of the femoral artery increased rather more. These increases occurred in spite of a fall in dry weight, attributed by the author to the accumulation of a water-rich mucoid substance. The calcium, cholesterol, and ash contents of the two arteries increased slowly until the fifth decade, after which the values for the femoral artery rose much more steeply than those for the brachial artery. For example, in the first decade of life the cholesterol content of the brachial artery per 100 g. wet weight was 126 mg. and of the femoral artery 124 mg.; in the fifth decade the figures were 217 and 246 mg., and in the eighth decade 256 and 648 mg. respectively.

The chemical composition of the right artery was compared with that of the left in 52 subjects. Up to the age of 40 years differences were insignificant, but between 40 and 80 years the right artery weighed more and contained more ash, cholesterol, and calcium than the left. In 52 diabetics aged 20 to 80 years there was an increase in all values. For example, between 20 and 40 years of age the right femoral artery in diabetics weighed twice as much and contained three times as much ash and cholesterol and six times as much calcium per unit wet weight as did the normal artery.
M. C. Berenbaum

636. **The Antemortem Diagnosis of Syphilitic Aneurysm of the Aortic Sinuses**
C. W. MERTEN, N. FINBY, and I. STEINBERG. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 345–360, March, 1956. 9 figs., 33 refs.

In this paper from the New York Hospital–Cornell Medical Center 9 cases in which syphilitic aortic sinus aneurysm was diagnosed during life by means of angiocardiography are reported. In 3 of the cases the condition was associated with syphilitic aortitis and saccular aneurysm and in 6 with aneurysmal dilatation of the aortic sinuses in continuity with a fusiform dilatation of the ascending aorta. The authors state that aortic sinus aneurysm should be suspected whenever there is syphilitic aortic regurgitation and linear calcification of the ascending aorta. "The diagnosis can be made with certainty if the calcification extends downwards and into the intracardiac origin of the aorta and the contour suggests dilatation of the aortic sinuses, or if there is massive calcification in this region. Angiocardiography affords confirmation of the diagnosis, the most informative view being the left anterior oblique."

In a series of 59 healthy subjects of the same age group as the patients the average width of the aortic sinus was 37 mm., range 30 to 49 mm. In the authors' 9 patients the average width was 62 mm., range 55 to 130 mm. It is pointed out that the prognosis in syphilitic aortic sinus aneurysm is not necessarily poor. Of the 9 patients, 2 are dead, 3 have been lost to observation, and 4 have been under observation for periods up to 5 years. All the survivors received penicillin therapy, and it is suggested that this may have been a factor in prolonging life. *L. G. Blair*

SYSTEMIC CIRCULATORY DISORDERS

637. **Hypertension and Associated Cardiovascular Disease**
R. H. SMITHWICK, R. D. BUSH, D. KINSEY, and G. P. WHITELAW. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1023–1026, March 24, 1956. 3 figs., 8 refs.

The five-year mortality rates have been obtained for 1,118 male and 1,109 female patients classified into four groups by a method of scoring objective cardiovascular findings. Group 1 contained patients with hypertension but no cardiovascular disease. Groups 2 and 3 contained patients with increasing degrees of damage in the cerebral, cardiac, or renal areas. Group 4 contained the patients with the most advanced cardiovascular changes. The tabulations show that the prognosis becomes worse as signs of cardiovascular–renal damage increase and that within each of the groups the prognosis for females with hypertensive cardiovascular disease is better than for males.

Patients treated surgically by a one-stage bilateral lumbodorsal splanchnicectomy are compared with patients receiving only medical treatment. The mortality rates were significantly better in all four groups of surgically treated male patients and in Groups 2 and 3 of the surgically treated female patients. In either sex the prognosis for Group 4 was shown to be poor. It is believed that patients of Groups 2 and 3 in general should be treated surgically, especially if medical treatment has been found ineffective after a trial of 8 to 10 weeks. —[Authors' summary.]

638. **Severe Hypertension—Study of One Hundred Patients with Cardiovascular Complications**
P. D. WHITE. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1027–1028, March 24, 1956. 1 ref.

A second follow-up report is presented on 100 hypertensive patients with cardiovascular complications, half of whom were subjected to Smithwick's lumbodorsal sympathectomy and the other half, matched as regards age and sex of the patients and nature of the complications, were treated by the orthodox medical measures used before the advent of the more powerful hypotensive drugs. None of the patients in these two groups suf-

fered from serious renal impairment when first seen. [For the first follow-up report see *J. Amer. med. Ass.*, 1950, **143**, 1311; *Abstracts of World Medicine*, 1951, **9**, 174.]

The present report emphasizes again the superior results obtained in the sympathectomized group. Of the 50 controls, 48 had died, the mean survival time of these 48 being 3·7 years and of the whole control group 4·1 years. In 4 cases the cause of death was not known; in 44 it was related to hypertension, 23 patients dying in congestive heart failure. Of the 50 patients subjected to sympathectomy, 25 had died, the mean survival time since operation of these 25 being 6·1 years and of the whole group 8·1 years. Death was due to congestive heart failure in 6 and to other complications of hypertension in 15. Of the surviving patients in this group, 20 were in good health, the blood pressure in 17 cases being substantially below the pre-operation level; of the remaining 5, 3 of whom were severely hypertensive, 4 were in fair health and one was in poor health.

H. F. Reichenfeld

639. **Treatment of the Ambulatory Hypertensive Patient with Pentolinium Tartrate. A Method for Regulating Dosage**

S. WALDMAN and L. PELNER. *American Journal of the Medical Sciences* [*Amer. J. med Sci.*] **231**, 140–150, Feb., 1956. 4 figs., 14 refs.

The authors begin by emphasizing the need for meticulous adjustment of the dosage of pentolinium tartrate given by mouth if the treatment of severe or moderately severe hypertension is to be successful. In a series of 26 patients studied at Long Island College Hospital, Brooklyn, New York, all of whom had a diastolic pressure over 110 mm. Hg and who had not responded to previous treatment, the authors' aim was to attain the lowest blood pressure consistent with comfort and the relief of symptoms.

The maximum fall in blood pressure was found to occur 2 to 3 hours after administration of the drug, which was given initially in doses of 10 to 20 mg. three times a day, the dose being later increased until the pressure was normal in the seated position and did not rise, or rose only slightly, on assuming the recumbent position—that is, the authors made use of the blocking effect of this manœuvre on the vasoconstrictor postural reflex. The drug was given half an hour before meals; if a higher dosage was required the evening dose was increased first, then the morning dose, and lastly the midday dose. The addition of reserpine (0·25 mg. three times a day) enabled smaller doses of pentolinium to be used and reduced the constipating effect of the latter. Constipation was avoided by the oral administration of neostigmine (15 mg. in the morning); the importance of this is stressed, since the presence of constipation leads to uneven absorption of the drug. Alcohol, a low-salt diet, and hot weather were found to potentiate the effect of pentolinium. Treatment was continued for periods ranging from 3 weeks to 11 months, and the authors found it " highly satisfactory ".

G. S. Crockett

640. **Pyretotherapy and Subcutaneous Hexamethonium in the Treatment of Severe and Malignant Hypertension**

P. THOMSEN, R. ORTÚZAR, F. GOÑI, C. ESPÍLDORA-LUQUE, and L. VIAL. *Circulation* [*Circulation* (*N.Y.*)] **13**, 351–359, March, 1956. 7 figs., 22 refs.

A report is presented from the Medical School of the Catholic University of Chile, Santiago, on 12 cases of severe and malignant hypertension treatment; was with subcutaneous hexamethonium, to which induction of fever by the injection of a mixed vaccine in doses sufficient to raise the temperature to 102° F. (38·9° C.) was added on 2 to 6 days in each week. Amidopyrine was also given to reduce distress from the fever. The number of pyrogenic injections varied from 12 to 46, depending on the patient's condition.

It was found that the dosage of hexamethonium needed was reduced and, quite apart from the immediate hypotensive effect of the drug, the blood pressure gradually fell to a more normal level. Moreover, treatment with pyrogens would restore the sensitivity to hexamethonium of patients who had become tolerant. Great improvement took place in the eye-grounds and electrocardiogram, as well as in the patient's symptoms. Complete cessation of treatment was followed by a return of the blood pressure to the previous level, but the improvement brought about by pyrogens could be maintained with a combination of hexamethonium and hydrallazine.

J. McMichael

641. **Livedo Reticularis with Ulcerations**

M. FELDAKER, E. A. HINES, and R. R. KIERLAND. *Circulation* [*Circulation* (*N.Y.*)] **13**, 196–216, Feb., 1956. 3 figs., 41 refs.

Idiopathic livedo reticularis may be associated with ulceration of the lower limbs, usually beginning during the winter. However, in reviewing the records of more than 400 patients with this diagnosis seen at the Mayo Clinic during the last 10 years the authors have discovered a number of cases in which the ulceration started only during the summer months. After fully reviewing the literature concerning livedo reticularis, they then proceed to describe 30 of the cases—18 with winter ulceration and 12 in which the ulceration started in the summer. In the patients with winter ulceration, hypertension, Raynaud's phenomenon, acrocyanosis, and thrombosis of the digital arteries were noted, whereas in those with the summer variety oedema of the legs and feet was a prominent feature. Histopathological study of biopsies taken at the ulcer sites in cases of summer ulceration revealed occlusion of the arteries and veins. Painful ulcers subsequently developed, which took months to heal. Treatment consisted of rest in bed, elastic supportive bandages to prevent oedema, and mild local therapy; one patient was also given hexamethonium. Sympathectomy was performed in some cases, but with little permanent effect.

Leon Gillis

642. **The Use of Aramine in Clinical Shock**

G. H. STECHEL, S. I. FISHMAN, G. SCHWARTZ, H. TURKOWITZ, P. F. MADONIA, and A. FANKHAUSER. *Circulation* [*Circulation* (*N.Y.*)] **13**, 834–836, June, 1956. 1 ref.

Haematology

643. **On Myelofibrosis**
D. R. KORST, D. V. CLATANOFF, and R. F. SCHILLING. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 169–183, Feb., 1956. 6 figs., 49 refs.

This paper from the University of Wisconsin, Madison, reports the findings in 23 cases of myelofibrosis in 15 male and 8 female patients, of whom 12 were over 60 years of age, while the youngest was 21 and the oldest was 73. The most frequent signs and symptoms were weakness, an abdominal mass, and pallor. All the patients had enlargement of the liver and spleen without significant lymphadenopathy, and 10 complained of sternal tenderness. They were almost all anaemic and the erythrocytes showed anisocytosis and poikilocytosis; normoblasts were present in the peripheral blood of all but one of the patients. The leucocyte count ranged between 2,000 and 200,000 per c.mm. and the neutrophil polymorphonuclear leucocytes showed a leukaemoid distribution. The platelet count was variable and abnormal forms of platelets were occasionally seen; in 15 cases circulating fragments of megakaryocytes were found. Aspiration of the bone marrow was attempted in 19 cases, but yielded nothing, or only sinus blood, while in further aspirated samples taken at different times or in different sites the picture was conflicting, since myelofibrosis is patchy and there are intervening areas of hyperplastic myelopoiesis.

A condition of myeloid metaplasia (extramedullary haematopoiesis) was established by biopsy or necropsy in 11 cases, but splenic and liver biopsies were not performed in all cases. Osteosclerosis was detected radiologically in 11 cases—in the femur in 8 and in the membranous bones in 3. It is pointed out that negative *x*-ray findings do not exclude the presence of myelofibrosis. An increased rate of haemolysis was common, the reticulocytes exceeding 3% in 16 cases and the faecal urobilinogen output being elevated in 9, while the erythrocyte survival time was shown with radioactive chromate to be abnormally short in 4 cases. The osmotic fragility of the erythrocytes was within normal limits. In 2 cases severe haemolytic anaemia improved after splenectomy, and the authors insist that this type of anaemia is the only indication for splenectomy in patients with myelofibrosis. Hyperuricaemia was present in 6 cases, not necessarily accompanied by a high leucocyte count, but only one patient had gout.

Irradiation of the spleen in 5 patients produced some symptomatic relief but did not influence the anaemia or the course of the disease, and prolonged therapy with "myleran" (busulphan) in 2 cases produced no benefit. Several of the patients died within 2 years, so that the prognosis is not necessarily better than in chronic granulocytic leukaemia; 4 patients in this series had polycythaemia vera and 5 had chronic granulocytic leukaemia. Myelofibrosis may exist at any stage of this leukaemia, even before therapy, and in the active or spent phase of polycythaemia vera. *T. B. Begg*

ANAEMIA

644. **The Distribution of Haemoglobin C in West Africa**
G. M. EDDINGTON and H. LEHMANN. *Man* [*Man*] **56**, 34–36, March, 1956. 3 gs., 23 refs.

Though the total proportion of abnormal haemoglobin carriers is similar in two groups from the northern and southern areas of the Gold Coast, a considerable difference is seen in the distribution of S and C haemoglobins, the latter being much more frequent in the northern group. The distribution of the C haemoglobin in Africa is discussed and it is suggested that it may be spreading from north to south in the Gold Coast and from there westwards into Nigeria.—[Authors' summary.]

645. **The Megaloblastic Anaemias**
R. H. GIRDWOOD. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 87–119, Jan., 1956. 3 figs., 46 refs.

The author, writing from Edinburgh University, describes the results of a study of over 1,000 cases of megaloblastic anaemia seen in the tropics, Great Britain, and the U.S.A., in some of which certain modern methods of investigation were used—namely, the differential test of urinary folic acid excretion and assay of the serum cyanocobalamin (vitamin B_{12}) level with *Lactobacillus leichmannii* as the test organism. [The capacity of the gastro-intestinal tract to absorb radioactive vitamin B_{12} was not studied.] The author considers that the nutritional megaloblastic anaemias form a complex group varying in aetiology in different parts of the world. Estimation of the serum vitamin-B_{12} level is of particular value in the diagnosis of Addisonian pernicious anaemia in patients who initially have nervous symptoms rather than the signs of haematological disease. In 49 out of 75 untreated cases of typical Addisonian pernicious anaemia the serum vitamin B_{12} level was below 50 $\mu\mu$g. per ml.; in the remainder it was below 130 $\mu\mu$g. per ml. In 120 patients without any cause for vitamin-B_{12} deficiency the level was 130 to 750 $\mu\mu$g. per ml. In megaloblastic anaemia due to malabsorptive diseases, such as idiopathic steatorrhoea, the results of the folic acid absorption test were more consistently and definitely positive than those of the fat-balance test, positive results being obtained in 28 out of 30 cases. In pernicious anaemia of pregnancy in patients whose diet was satisfactory—that is, in Britain as opposed to the tropics—the serum vitamin-B_{12} level and absorption of synthetic folic acid were normal; the author suggests, however, that there is present some unrecognized disturbance of folic acid metabolism. Low serum vitamin-B_{12} levels were observed in patients after total or partial gastrectomy and after gastro-enterostomy, while folic acid absorption was normal. If blind or stagnant loops were present administration of the vitamin was successful in some cases in controlling the anaemia.

The author discusses one case of megaloblastic anaemia due to chronic liver disease, one of epilepsy in which anaemia developed on two occasions during treatment with phenytoin or primidone, and cases of unexplained refractory anaemia. *Janet Vaughan*

646. **Radioactive Tracer Tests for the Recognition and Identification of Vitamin B_{12} Deficiency States**
J. R. KREVANS, C. CONLEY, and M. V. SACHS. *Journal of Chronic Diseases* [*J. chron. Dis.*] **3**, 234–252, March, 1956. 4 figs., 28 refs.

From the Johns Hopkins University School of Medicine and Hospital are reported over 100 studies of cyanocobalamin (vitamin B_{12}) absorption in 92 patients, vitamin B_{12} labelled with radioactive cobalt being given in a dose of 0·1 to 5 μg. In one study of the relationship between the amount of radioactive vitamin administered and the fraction recovered from the faeces the authors state that the percentage of the administered dose recovered was not significantly altered when the dose was reduced from 0·5 μg. to as low as 0·1 μg.; on the other hand when the dose was increased to 1 μg. a much larger percentage was recovered.

Impaired absorption of vitamin B_{12} was observed in patients with Addisonian pernicious anaemia, sprue, regional ileitis, and jejunal diverticulosis, and after total gastrectomy or resection of large portions of the small intestine. Administration of an antibiotic improved absorption in a patient with jejunal diverticulosis, presumably by eliminating bacterial competition for the vitamin. Administration of an intrinsic-factor preparation corrected the absorption deficiency in pernicious anaemia and after total gastrectomy, but was without effect in the other disorders.

Janet Vaughan

647. **Type-specific Cold Auto-antibodies as a Cause of Acquired Hemolytic Anemia and Hemolytic Transfusion Reactions: Biologic Test with Bovine Red Cells**
A. S. WIENER, L. J. UNGER, L. COHEN, and J. FELDMAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 221–240, Feb., 1956. 29 refs.

The authors describe a case of acquired haemolytic anaemia in which cold auto-antibodies in extremely high titre were detected in the patient's serum. This case exhibited certain important differences of fundamental significance from similar cases reported in the past.

The patient, a woman aged 62, had first been treated for severe haemolytic anaemia 3 years after undergoing cholecystectomy, which was complicated by multiple lung abscesses; during this illness she had received 6 one-pint (0·6-litre) transfusions of blood and had been told after the last that she would never be able to receive another transfusion. When first seen by the authors a year later the most conspicuous abnormal haematological finding, apart from severe anaemia, was a tendency for her erythrocytes to undergo spontaneous massive clumping. Tests confirmed the presence in her serum of a cold auto-antibody in high titre. She was transfused successfully with warmed blood of her own group (AB MN Rh_2), but eventually had violent haemolytic transfusion reactions. These were explained by the discovery that the cold auto-antibodies in the patient's serum were to a certain degree type-specific at room temperature. Amongst 22,000 blood donors, 5 were found whose blood was compatible with the patient's serum and could be safely transfused after warming, with great benefit to the patient. The factor detected by this patient's serum, which is of almost universal distribution, was found to be different from any previously described blood factor in human blood and has been designated the I factor. Because of the difficulty of obtaining a compatible donor, a biological test with bovine erythrocytes washed thoroughly with saline was tried, 50 ml. of a 50% suspension being injected intravenously. No haemolysis resulted, but an anaphylactoid reaction discouraged further experiments. The patient experienced remissions of variable length after transfusion from compatible donors, but ultimately clumping of the erythrocytes in the blood vessels of the brain occurred during an acute haemolytic crisis and she died.

In titrations of the patient's serum at room temperature with unmodified erythrocytes the titre for I-positive erythrocytes was as high as 5,000 units, but reactions were obtained indicating the existence of subgroups I_1, I_2, and I_3. Attempts to separate the anti-I agglutinin from the cold auto-antibody by absorption were unsuccessful, indicating that a single cross-reacting antibody was involved, as in the group-specific reactions obtained with bean agglutinins.

It is now considered that acquired haemolytic anaemia comprises two distinct immunological entities. In the one the auto-antibodies are of autologous origin, react at body temperature, and have properties similar to those of the Rh antibodies, while in the other the auto-antibodies appear to be of heterologous origin and react at low temperatures, as in the case described. Evidence is presented to suggest that the latter variety may occur chiefly in I-negative individuals. *A. Ackroyd*

648. **Acquired Haemolytic Anaemia. Clinical and Serological Observations of Two Cases**
W. WEINER, J. P. WHITEHEAD, and W. J. WALKDEN. *British Medical Journal* [*Brit. med. J.*] **1**, 73–77, Jan. 14, 1956. 14 refs.

The authors, writing from the Birmingham Blood Transfusion Service, describe the clinical and serological findings in 2 patients suffering from acquired haemolytic anaemia. The first patient had radiological evidence of patchy infiltration of the left upper lobe of the lung, and the possibility of a common viral aetiology for both the pneumonia and the haemolytic anaemia is discussed. The second patient was suffering from thrombocytopenia in addition to acquired haemolytic anaemia. The condition in both cases was controlled by the administration of cortisone.

An anti-E antibody was found in both the cases, both in the serum and in the eluate from the erythrocytes. In the second patient anti-c was, in addition, detected in the eluate, but not in the serum; in this case transfused blood was apparently rapidly destroyed. The theoretical

and practical effects of blood transfusion in acquired haemolytic anaemia are discussed, and the difficulty of selecting suitable blood is pointed out. The authors recommend, in the light of their findings, that in the performance of blood compatibility tests in cases of acquired haemolytic anaemia the eluate should be used for cross-matching in addition to the serum.

J. L. Markson

HAEMORRHAGIC DISEASES

649. **Use of Prednisone in the Management of Some Hemorrhagic States**

M. STEFANINI and N. B. MARTINO. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 313–317, Feb. 16, 1956. 4 figs., 19 refs.

Because cortisone in large doses often causes unpleasant side-effects, prednisone in a dosage of 0·8 to 1·6 mg. per kg. body weight has been tried at Saint Elizabeth's Hospital, Boston, in the treatment of some haemorrhagic states. In 6 cases of primary thrombocytopenic purpura the haemorrhagic phenomena were well controlled, although the effect on the platelet count was variable and possibly less good than that of cortisone. Prednisone also controlled haemorrhage in the secondary thrombocytopenia of acute leukaemia (4 cases). In 2 patients with aplastic anaemia there was partial control of bleeding but no reduction in the need for blood transfusion. An apparent remission was obtained in 2 cases of acute anaphylactoid purpura, but there was no effect in one chronic case. The most striking results were observed in 7 patients with " vascular pseudohaemophilia " (von Willebrand's disease), in whom the bleeding time was reduced. In spite of the large doses employed, side-effects of the drug were slight and in no case necessitated cessation of treatment.

P. C. Reynell

650. **Thrombotic Thrombocytopenic Purpura. A Hyperergic Micro-angiopathy**

A. E. STUART and G. MACGREGOR-ROBERTSON. *Lancet* [*Lancet*] **1**, 475–479, April 21, 1956. 4 figs., 32 refs.

651. **Haemorrhagic Diatheses and the Activity of the Antihaemophilic Factor in Women.** (Diathèses hémorragiques et activité du facteur antihémophilique chez la femme)

M. VERSTRAETE and J. VANDENBROUCKE. *Revue d'hématologie* [*Rev. Hémat.*] **10**, 665–673, 1955. 2 figs., 15 refs.

The authors, writing from the University of Louvain, describe a case of true haemophilia in a girl aged 6 years in whom the condition had apparently been present from birth. Her parents were not related and neither they nor the grandparents had any history of a bleeding diathesis. One of the patient's sisters died early in infancy from haemorrhage, one brother (now aged 15 years) has true haemophilia with diminished plasma anti-haemophilic globulin (A.H.G.) content, while the remaining 2 sisters and one brother are normal. The thromboplastin generation test, the bleeding and coagulation times, plasma recalcification time, and plasma heparin tolerance test all gave abnormal results in the patient and her affected brother, a deficiency of A.H.G. being found in both cases. The presence of an endogenous circulating anticoagulant inhibiting the action of A.H.G. was excluded.

The authors also describe the case of a woman, aged 61 years, who gave a history of bleeding which had begun one to 2 years previously. Bleeding time and the result of the thromboplastin generation test were both abnormal, whereas the plasma recalcification time and coagulation time were normal. In this case also there was a deficiency of A.H.G., which was confirmed by the failure of the plasma to correct the coagulation time of haemophilic blood, and its ability to do so in blood from a patient with Christmas disease. The condition in this case, being acquired, was not true haemophilia. There was no circulating anticoagulant. The authors postulate the existence of some vascular defect.

M. Lubran

NEOPLASTIC DISEASES

652. **Myelofibrosis and Osteomyelosclerosis. The Osteomyeloreticulosis Syndrome.** (Myelofibrose und Osteomyeloskerose. (Osteomyeloretikulose-Syndrom))

K. ROHR. *Acta haematologica* [*Acta haemat.* (*Basel*)] **15**, 209–234, April, 1956. 11 figs., 50 refs.

The syndrome of myelofibrosis is characterized by splenomegaly, the presence of immature cells, striking poikilocytosis, and giant platelets in the peripheral blood, and fibrosclerosis of the bone marrow, often with osteosclerosis, and is usually associated with extramedullary haematopoiesis in the spleen, liver, and lymph nodes. The present author discusses a series of 20 cases conforming to this definition, 12 of which were examined post mortem at the Zürich Pathological Institute, while biopsy specimens of the bone marrow were examined in 4 others. The sex distribution was equal, the patients' ages ranged from 40 to 70 years, and the duration of the illness from 1 to 14 years. In some cases the spleen was already huge at the time advice was first sought, and in these the course was short. The 3 cases with the longest survival presented with polycythaemia 10 to 15 years before the final phase of the illness. In 7 of the author's cases the blood picture was leukaemoid, while in 3 cases the disease was of a neoplastic character, one resembling Hodgkin's disease, one showing granulomatous foci in the head of the femur and in the serous membranes, and one having an enormous tumour originating in the mesenteric lymph nodes, the histological examination of which showed intense fibrous-tissue proliferation with reticulin and collagen fibrils, giant cells, and numerous blast cells. In 8 cases febrile episodes occurred which responded to cortisone but not to antibiotics. Cirrhosis of the liver was found in 5 cases. Splenectomy was performed on 4 patients, who survived 3 months, 9 months, 2 years, and 4 years respectively.

The pathogenesis of myelofibrosis is discussed in relation to the theories currently prevailing. The author considers it to be an irreversible, progressive, prolifera-

tive condition with a tendency to cellular dedifferentiation and would place it among the neoplastic reticuloses. He suggests that the term "osteomyeloreticulosis" is more suitable than myelofibrosis, since the condition originates in the reticulo-histiocytic system of myelopoietic organs. Its development may be attributable to a tumour *Anlage*—possibly due to genetic or to viral factors acting in early embryonic life. Later on, a precipitating "realization factor" may exert a contributory effect. *F. Hillman*

653. **Therapy of the Malignant Lymphomas. I. A Study of 116 Cases. II. A Review**
C. A. Hall and K. B. Olson. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 392–398 and 399–411, March, 1956. 49 refs.

In the first part of this paper from Albany Medical College, New York, the authors review certain findings in 116 cases of malignant lymphomata (66 of Hodgkin's disease, 39 of lymphosarcoma, 7 of follicular lymphoma, and 4 of reticulum-cell sarcoma), with particular reference to the value in treatment of nitrogen mustard. A few of the patients were not treated or underwent operation; the remainder received *x*-ray therapy only, or nitrogen mustard only, or a combination of these two, a course of *x*-ray therapy being followed by a course of nitrogen mustard and vice versa. Full details of the response to treatment in each case are given, including the duration of remissions and the final outcome. It was found that the results with nitrogen mustard alone were very similar to those with irradiation alone; there were, however, wide variations between individual patients. It was also found that if a patient was resistant to one form of therapy he was also resistant to the other, and that the treatment given in the first phase, whether irradiation or nitrogen mustard, was usually the more effective. The response in the present series of cases was evaluated from the number and duration of remissions, not from reduction in size of the tumour mass, speed of response, or degree of toxicity to the agent used. A comparison of the results with those obtained in an earlier series, before nitrogen mustard therapy was used, suggests that there were more short remissions in patients receiving both nitrogen mustard and *x*-ray therapy than in patients receiving *x*-ray therapy alone.

The second part of the paper is devoted to an analysis of the results obtained with different agents in the treatment of malignant lymphomata, as reported in the literature; the authors' conclusions from this analysis may be summarized as follows. Localized lymphosarcoma and reticulum-cell sarcoma are curable in some instances, especially if the primary focus is in a viscus. There is, however, no conclusive evidence that localized Hodgkin's disease can be cured. Surgery and irradiation have been equally effective in the treatment of localized lymphosarcoma. Except for these occasional apparent cures there is no proof that *x*-ray therapy has prolonged the life of patients with any of the lymphomata, although some reports do suggest a prolongation of life. There is no doubt, however, that treatment results in symptomatic improvement. Nitrogen mustard relieves symptoms and reduces the size of the tumour in all cases of lymphomata, but the duration of remission from a single course of nitrogen mustard is shorter than that following a course of irradiation. However, the information available does not permit an accurate comparison of the effect of these two agents on the over-all course of the disease. A combination of irradiation and nitrogen mustard appears to be the most efficacious form of treatment, but the survival rate is the same as that observed after irradiation alone. The therapeutic effect of triethylene melamine (TEM) is similar to that of nitrogen mustard, but the depressant effect on the bone marrow of TEM by mouth is less predictable than that of nitrogen mustard. Patients with advanced disease often obtain some symptomatic relief from cortisone or ACTH. These hormones may decrease haemolysis in patients with a secondary haemolytic anaemia and may increase haematopoiesis in patients with hypocellular bone marrow.

Finally, the authors state that no definite conclusions can be reached concerning these therapeutic agents in lymphosarcoma, partly because methods of study are inadequate and are not standardized. In their view the establishment of basic principles of methods of study and better organization of effort would increase the value of future investigations. *R. F. Jennison*

654. **Myleran in Treatment of Chronic Myeloid Leukaemia**
E. K. Blackburn, G. M. King, and H. T. Swan. *British Medical Journal* [*Brit. med. J.*] **1**, 835–837, April 14, 1956. 8 refs.

A detailed study is presented of 18 cases of chronic leukaemia treated with "myleran" (1:4-dimethanesulphonyloxybutane) at the Royal Infirmary, Sheffield. The dosage used in most cases was 0·06 mg. per kg. body weight, larger doses having given rise to thrombocytopenia in several of the cases treated first. The drug was given as long as clinical and haematological improvement continued. In some cases *x*-irradiation of the splenic area was also given. Of 8 cases not previously treated, 7 of myeloid leukaemia had satisfactory remissions, the eighth being a case of neutrophilic leukaemia. Of 10 cases, all of myeloid leukaemia, which had previously received radiotherapy, a satisfactory remission was obtained in 7, including 4 of the 6 radioresistant cases. There was a rather high incidence of acute relapse, which was the cause of 7 of the 13 deaths, and resistance to the drug sometimes developed, but it is suggested that both relapse and drug resistance are less likely to occur with interrupted than with continuous courses.

The question whether treatment with this drug is an effective substitute for radiotherapy is left open, because no case had been observed for more than 3 years, which is approximately the average survival time. The authors consider, however, that myleran, while not superior to radiotherapy, is preferable to other chemotherapeutic agents (with the possible exception of demecolcine) for the treatment of radioresistant cases of chronic myeloid leukaemia or when radiotherapy is not available.
A. Piney

Respiratory System

655. **Bronchiolar Disease in Chronic Pulmonary Emphysema.** (Le rôle de l'atteinte bronchiolaire dans l'emphysème pulmonaire chronique)
R. KOURILSKY, S. KOURILSKY, R. LAURENT, J. CHEVREAU, D. BRILLE, and C. HATZFELD. *Presse médicale* [*Presse méd.*] **64**, 324–328, Feb. 22, 1956. 8 figs., bibliography.

The authors of this paper from the Hôpital Saint-Antoine, Paris, attempt to draw a complete picture of the syndrome of bronchitis and emphysema from a study of 14 cases. Of these, both clinical and pathological details were available in 8 cases, in 2 of which complete and in 3 partial investigations of pulmonary function had been carried out; in the remaining 6 cases only the clinical details and results of pulmonary function tests were available. They emphasize the importance in the evolution of the disease of expectoration, which indicates hypersecretion of mucus by the bronchi. They also emphasize the pathological evidence of bronchiolar obstruction and alveolar degeneration and conclude that the obstruction is responsible for the functional abnormalities which they observed. They comment on the foresight of Laënnec, who, as long ago as 1826, attributed the development of emphysema to bronchiolar obstruction.

C. M. Fletcher

656. **Respiratory Function in Emphysema in Relation to Prognosis**
D. V. BATES, J. M. S. KNOTT, and R. V. CHRISTIE. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **25**, 137–157, Jan., 1956. 13 figs., 17 refs.

An analysis of the sequence of the functional changes in the lungs in emphysema is presented as the result of regular clinical out-patient supervision, with serial lung function tests, of a group of 59 patients observed over an average period of three years at St. Bartholomew's Hospital, London. These patients represent those who attended regularly out of 88 patients with emphysema diagnosed clinically on the grounds of increasing exertion dyspnoea, constantly present for years, with no other apparent cause. Their symptoms and degree of dyspnoea, divided into 5 grades on the basis of clinical history, were recorded independently of the results of functional tests, which included closed-circuit measurement of total lung capacity and " gas-mixing efficiency ", maximum voluntary ventilation, and diffusing capacity at rest as measured by carbon monoxide uptake. All the test results showed similar trends, but only the estimation of carbon monoxide uptake indicated those patients who had a poor prognosis in that they died within 6 months of the last test. Death occurred from pulmonary heart failure in 8 cases (13%) within 2 years, and in 13 (22%) within 4 years. Histological evidence of advanced emphysema was found in all 9 patients who came to necropsy.

The authors conclude that there are two distinct processes in emphysema, running concurrently: reduction of ventilatory capacity, mainly responsible for dyspnoea, and reduction of pulmonary capillary bed, which may not give rise to symptoms until it leads to heart failure. The latter is assessed by measuring the diffusing capacity of the lungs, which is the best guide to prognosis.

[This valuable paper should be read in full. The authors' conclusion in the summary that bronchial obstruction is mainly responsible for the dyspnoea, although undoubtedly true, may possibly underemphasize other causes of reduced ventilatory capacity.]

P. Hugh-Jones

657. **The Effects of the Carbonic Anhydrase Inhibitor Acetazoleamide on Chronic Respiratory Acidosis.** [In English]
M. M. PLATTS and T. HANLEY. *Acta medica Scandinavica* [*Acta med. scand.*] **154**, 53–64, March 8, 1956. 3 figs., 23 refs.

The authors report, from the University of Sheffield, the effects of prolonged acetazolamide therapy on the acid–base balance of 7 patients with chronic respiratory acidosis who were given the drug in a single daily dose of 0·25 g., or 1·5 g. daily in divided doses, for periods of 3 months to one year. No noticeable clinical improvement resulted, nor on the other hand were toxic effects troublesome. The following biochemical events took place: (1) a large excretion of bicarbonate in the urine began immediately after the start of treatment and lasted about 4 days, but thereafter ceased although the administration of acetazolamide was continued; (2) there was a reciprocal fall in the plasma bicarbonate level at the beginning of treatment and this value remained at a lower and fairly constant level throughout treatment. The arterial pCO_2 fell, but this fall was sometimes relatively less than that of the plasma bicarbonate level. The *p*H of the blood tended to fall or remained unchanged. In this phase of chronic acidosis the urine was of normal composition. The pre-treatment level of acidosis could be restored by hyperventilation.

The authors believe that the metabolic acidosis produced by acetazolamide is generally compensated for by increased pulmonary excretion of CO_2. The efficiency of such compensation depends upon pulmonary factors and is not influenced by acetazolamide itself.

Bernard Isaacs

658. **Surgery for Metastatic Neoplastic Disease in the Lung. Review of 38 Cases**
L. K. GROVES and D. B. EFFLER. *Cleveland Clinic Quarterly* [*Cleveland Clin. Quart.*] **23**, 16–27, Jan., 1956. 3 figs., 2 refs.

From surgical experience in 38 cases of metastatic neoplastic disease in the lung (diagnostic biopsy in 9 cases, palliative resection in 4, and curative operations in 25) the authors group the indications for surgery as follows: (1) diffuse disease, biopsy being a planned minimal diagnostic procedure; (2) solitary circum-

scribed "coin" lesion; (3) suspected solitary neoplastic metastasis; (4) presumed primary pulmonary neoplasm; and (5) metastatic neoplastic lesions obstructing a bronchus (palliative procedure only). In the 25 cases in which curative operations were performed the indications were those of Groups 2, 3, and 4, exploratory thoracotomy and biopsy only being carried out in 11, lobectomy or enucleation of the tumour in 9, and pneumonectomy in 5. Of the 9 patients subjected to lobectomy, 8 were alive 1 to 5½ years later, 2 having had a second operation for contralateral metastases. The survivors included 2 patients with primary haemangiopericytomata, 2 with carcinoma of breast, and 4 with renal, ovarian, salivary, and intestinal tumours respectively.

A radical approach in these cases is advised, the authors holding the view that the longer the interval between treatment of the primary growth and the appearance of a secondary tumour, the better the prognosis. *C. A. Jackson*

659. **Corticotrophin in Treatment of Acute Exacerbations of Chronic Bronchitis**

D. Felix-Davies and E. K. Westlake. *British Medical Journal* [*Brit. med. J.*] **1**, 780–782, April 7, 1956. 1 fig., 11 refs.

In cases of chronic bronchitis exacerbated by an acute respiratory infection the mortality is high in spite of the use of appropriate antibiotics. Acute respiratory failure in these cases is considered to be due chiefly to bronchial obstruction brought about by spasm, oedema, and increased secretion following the acute inflammation. At the Postgraduate Medical School of London the authors tried corticotrophin in the treatment of 24 patients suffering from an exacerbation of chronic bronchitis; all received routine treatment with antibiotics, antispasmodics, stimulants, and oxygen, but 12 were given in addition 15 units of corticotrophin gel intramuscularly every 6 hours for 6 days (with a lower dosage for a further 2 days). No evidence of any beneficial effect was observed in the 12 patients receiving corticotrophin. There were 2 deaths in the control group and 3 in the treated group. Bronchial obstruction, as assessed by the maximum voluntary ventilation test, improved equally in the two groups. It is concluded that corticotrophin is of no value in such cases.

K. C. Robinson

660. **The Surgical Treatment of Pulmonary Histoplasmosis, with an Evaluation of MRD-112 as a Possible Adjunct**

J. W. Polk, C. A. Brasher, J. DeCastro, and W. W. Buckingham. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **31**, 148–162, Feb., 1956. 5 figs., 18 refs.

The clinical features of pulmonary histoplasmosis and its similarity to chronic fibrocaseous tuberculosis are discussed briefly and 12 cases treated at the Missouri State Sanatorium, Mount Vernon, all but 2 of them in males, are described. The patient's ages ranged from 37 to 62 years and the duration of the disease from 6 to 67 months. The disease was confined to the upper lung fields in 8 cases and was bilateral in 4 (in 2 with destruction of the left lung and right apical infiltration). The lesions were fibrocaseous in 11 cases and solid in one. Concomitant pulmonary tuberculosis was present in 2 cases.

Treatment was surgical in 7 cases and medical in 5. "MRD-112" (β-diethylaminoethyl fencholate), an experimental antifungal agent, was given in all of the latter and in one of the former, 150 mg. being injected intravenously daily for 60 days in the surgical case and for an unspecified period in the others. The response to medical treatment was very disappointing, none of 6 patients treated with MRD-112 deriving any benefit, while 3 became worse and 5 showed signs of varying degrees of liver damage. The results of surgery were promising and all 5 patients who survived surgery have returned to normal life. Right pneumonectomy was carried out in one case, bilateral segmental resection in 2, lobectomy in 2, wedge resection in one, and thoracotomy in one. One patient died on the 10th day after right upper lobectomy from pulmonary embolism, and one on the 3rd day after thoracotomy from acute enteritis, toxic hepatitis, and toxic nephritis; this patient had received preliminary treatment with MRD-112.

Co-existent pulmonary tuberculosis is not uncommon in cases of histoplasmosis, and preoperative antituberculous chemotherapy is justified in such cases. Serological studies have been found useful in assessing the activity of the disease. It is suggested that operation be withheld until the complement-fixation reaction indicates stabilization of the disease, or until its strength is 1:8 or less. *F. J. Sambrook Gowar*

661. **The Localized Pleural Effusion.** (Der lokalisierte Pleuraerguss)

K. Heckmann. *Fortschritte auf dem Gebiete der Röntgenstrahlen und der Nuklearmedizin* [*Fortschr. Röntgenstr.*] **84**, 176–184, Feb., 1956. 11 figs., 15 refs.

Localized pleural effusions are not uncommon, in the author's opinion, but are less frequently diagnosed than those in the free pleural space as their radiographic demonstration needs a special technique. Such effusions may be interlobar, diaphragmatic, mediastinal, or apical. The space in which the exudate accumulates does not necessarily correspond with the exudative zone of the pleura. A case is cited in which an effusion accumulated as a result of reduced intrapleural pressure over an area served by bronchi which were slightly stenosed, and other cases in which exudates were sucked into the apical area because of contraction atelectasis of a cavity in the upper lobe and into the upper paramediastinal space owing to collapse of the upper lobe. Whether the exudate is held in position by anatomical changes or only by suction can be demonstrated by examination in expiration and inspiration when, if the exudate is not encapsulated, it will be visible in different pleural areas in the two films.

The author also describes what he calls the "halo phenomenon", in which the borders of the heart appear unsharp owing to overlying paracardial effusions in the anterior mediastinum. *M. E. Grossman*

Otorhinolaryngology

662. **Hypometabolism in Relation to Ear, Nose, and Throat Disorders**
A. R. HOLLENDER. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **63**, 135–141, Feb., 1956. 32 refs.

In a study of 202 cases of vasomotor rhinitis, postnasal discharge, deafness, tinnitus, lymphoid hyperplasia of the pharynx, and headache, carried out at the University of Miami School of Medicine, more than half the patients in each group were found to have a subnormal basal metabolic rate (B.M.R.), and more than half of these in each group improved under thyroid treatment. The author believes that thyroid deficiency may exist without obvious clinical signs. He regards the B.M.R. as the most useful of the various laboratory tests for its detection. In addition, determination of the blood protein-bound iodine level may reveal the presence of hypothyroidism, while an increase in the plasma cholesterol level may also be significant. The literature is reviewed and freely quoted. In the present study, of 52 patients with vasomotor rhinitis a low B.M.R. was found in 38, and in 18 of these there was also a low protein-bound iodine level. Lymphoid hyperplasia of the pharynx may be due to endocrine dysfunction, especially hypothyroidism. Headache in cases of vasomotor rhinitis in which the B.M.R. is low also responds to thyroid medication. In treatment the author found that increasing doses were not needed, and that when the defect had been corrected the dosage could be gradually reduced to a low maintenance level, and the administration of thyroid eventually discontinued.

F. W. Watkyn-Thomas

663. **Some Aspects of Fenestration**
F. HARBERT. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **63**, 347–350, April, 1956. 2 figs.

664. **Chronic Otitis in Children**
J. BOURDIAL and J. J. DEBAIN. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol. (St Louis)*] **65**, 57–67, March, 1956. 4 figs.

The authors divide chronic otitis in children into the following groups: (1) Mucous otorrhoea, where the perforation is in the lower part of the pars tensa and does not involve the edge of the drum. Treatment is removal of the adenoids and sinus irrigation by displacement, with irrigation of the ear followed by insufflation of antibiotics. (2) Attico-tympanic mucopurulent otorrhoea, in which there is a perforation in the paracentral region or postero-superior quadrant. For this type medical treatment is recommended, with a limited attico-antrotomy if the infection persists. (3) Attic suppuration, which requires attico-antrotomy and removal of the incus and head of the malleus. (4) A large kidney-shaped perforation. Various kinds of infection may cause this, as well as cholesteatoma. If operation is required, attico-antrotomy should be performed.

Considering that simple mastoidectomy is ineffective and the radical procedure too severe, the authors make a plea for simple limited operation (atticotomy) in all cases of chronic otitis in children, irrespective of age.

William McKenzie

665. **An Unusual Case of Sphenoid Abscess**
C. C. CODY. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **63**, 199–202, Feb., 1956. 4 figs., 7 refs.

In the case here reported from Baylor University College of Medicine, Houston, Texas, the ostium of the right sphenoid sinus was entirely occluded by bone, and an abscess had formed in it without involvement of any other sinus. Intense pain in the right eye and temple was followed by swelling and protrusion of the eye. Radiography revealed a shadow near the right eye, which was diagnosed as an aneurysm. The pain receded for 3 months but then recurred, and a neurosurgeon performed partial ligation of the internal carotid artery, with relief of pain for another 3 months. However, symptoms again recurred and the artery was tied off inside the skull, but this brought no relief. Later, during a last attempt to remove the supposed aneurysm, the anterior clinoid process was accidentally fractured, opening the roof of the sphenoidal sinus from which thick pus then escaped. Thereafter the patient came under the care of the author, who exposed the ethmoid by external incision and opened and drained the sphenoidal sinus. It contained over 15 ml. of fluid, and the lining was gangrenous and necrotic, with underlying rough bone. The patient is now gradually improving. The author remarks that if proper radiographs had been taken and properly interpreted the patient would have been saved 2 years of pain and a series of needless operations.

F. W. Watkyn-Thomas

666. **Wegener's Granulomatosis**
C. W. HOCH. *A.M.A. Archives of Otolaryngology* [*A.M.A. Arch. Otolaryng.*] **63**, 120–123, Feb., 1956. 15 refs.

Wegener's granulomatosis is a rare condition characterized by necrosing granulomatous lesions in the respiratory tract, with generalized necrosing angiitis and glomerulonephritis; it was first described in 1931 by Klinger, although Wegener later (1939) established it as a disease entity. There is disagreement as to whether the nasal lesions are pathognomonic or whether involvement of an unspecified part of the respiratory system is more distinctive. The present author describes 2 cases. In one, in a negro woman aged 51, the first diagnosis was tuberculous pleuritis and the patient was treated for 6 months with streptomycin, and only then was she

referred to the otolaryngological department for deafness, when an irregular mass in the middle meatus was observed. Biopsy examination showed chronic granulomatous inflammation. A month later there was recurrence of the chest symptoms, but no apparent change in the nasal mass. Biopsy of the gastrocnemius muscle showed necrosing arteriolitis, and blood cells and albumin were found in the urine. After a course of nitrogen mustard, however, the patient became symptom-free and was discharged from hospital.

In the second case, in a man aged 54, a bronchoscopic biopsy showed chronic inflammation and granuloma in the right upper lobe of the lung. Thoracotomy revealed a mass which seemed to be neoplastic, and pneumonectomy was performed. However, 2 months later crusting and bleeding in the nose were noticed; after another 5 months the nasal state had greatly deteriorated, and radiography showed patchy changes in the left lung. The patient died a few days later, and necropsy revealed granulomatous lesions in the nose, nasopharynx, and left lung, as well as glomerulonephritis, but no involvement of blood vessels and no necrosing angiitis. The first case seemed to fit Wegener's description of the disease, but the second was difficult to classify, since the typical angiitis of Wegener's disease was not present. The author suggests that lethal midline granuloma, Löffler's syndrome, and the "allergic angiitis and granulomatosis" described by Churg and Strauss, as well as periarteritis nodosa, may all be manifestations of a single common condition, the basis of which may be some form of hypersensitivity.

F. W. Watkyn-Thomas

667. **On the Treatment of Maxillary Sinusitis with Oxytetracycline and Penicillin**
J. S. LUMIO. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 52–58, Jan., 1956.

The object of the investigation described in this paper from the Institute of Occupational Health, Helsinki, Finland, was to determine whether maxillary sinusitis could be cured by treatment with antibiotics (oxytetracycline or penicillin) without maxillary puncture, which was not performed even for diagnostic purposes. To 106 patients with maxillary sinusitis oxytetracycline was given to a total of 16 capsules of 250 mg. each over a period of 5 days, while 102 similar patients received 450,000 units of procaine penicillin daily for 5 days. After one week's treatment 78·3% of the patients given oxytetracycline and 30·4% of those given penicillin were subjectively symptom-free. However, purulent or mucopurulent secretion was observed on maxillary puncture in 16% of the oxytetracycline-treated group and 48% of the penicillin-treated group. At a follow-up examination after 3 months 90·6% of the former and 86·3% of the latter group were symptom-free. Penicillin did not cause any side-effects, but 6·7% of the patients treated with oxytetracycline had a dermal pruritus or eczema and 34·9% had diarrhoea. Nevertheless, the author considered that in spite of this higher incidence of side-effects the therapeutic results were considerably better with oxytetracycline than with penicillin.

[The type of maxillary sinusitis treated, whether acute, subacute, or chronic, is not indicated. To diagnose active maxillary sinusitis on the radiological appearances only (except in cases in which there is a fluid level) without a diagnostic puncture is taking a good deal for granted.] *E. D. Dalziel Dickson*

668. **Indications for Radical Surgery, Partial Surgery, Radiotherapy and Combined Surgery and Radiotherapy for Cancer of the Larynx and Hypopharynx**
J. LEROUX-ROBERT. *Annals of Otology, Rhinology and Laryngology* [*Ann. Otol.* (*St. Louis*)] **65**, 137–153, March, 1956. 6 figs., 14 refs.

On the basis of 800 cases of cancer of the larynx and hypopharynx operated on during the past 18 years at the Curie Foundation, Paris, the author attempts to postulate therapeutic indications for the different anatomical varieties of the disease. When the cancer is limited to a small area in the middle of a vocal cord he advises surgical removal of the cord. When it involves the whole cord, if the cord is still mobile, surgery and radiotherapy are equally successful and cure should be complete; but if cord movement is impaired, surgery is preferable to radiotherapy. A hemilaryngectomy in these cases is usually adequate, the 5-year cure rate being about 70%. Involvement of the vocal cord in the anterior commissure requires surgery, which is strongly to be preferred to radiotherapy. In subglottic carcinoma surgery, usually total laryngectomy, is needed unless the disease is strictly unilateral, when a Hautant type of hemilaryngectomy is adequate. With the latter operation a cure rate of 70% has been obtained. Cancer of the ventricle is better treated by surgery than by radiotherapy, the operation required being total laryngectomy, which has given a 5-year cure rate of 30 to 35%. In cancer of the ventricular bands and laryngeal surface of the epiglottis the best results have been obtained with total laryngectomy followed by a full course of radiotherapy, the addition of radiotherapy having increased the 5-year cure rate to nearly 30%. Radiotherapy without surgery has been just as successful in some of these cases, provided the growth was superficial and did not extend deeply.

The author has never seen metastatic lymph-node enlargement in cancer of the vocal cord or anterior commissure, and only one lymph-node metastasis has occurred among 100 cases of subglottic cancer. On the other hand lymph-node metastasis is common in vestibular cancer. Where there is a single enlarged lymph node total laryngectomy with a block dissection is advised. If more than one enlarged lymph node is present radiotherapy is to be preferred, followed by surgery if necessary; but if there is no response to radiotherapy surgery will prove equally useless. Both radiotherapy and surgery have in the past given disappointing results in cancer of the aryepiglottic fold and of the pyriform sinus, in the majority of which enlarged lymph nodes develop. In these cases the author has tried combinations of surgery and radiotherapy, and though his results are encouraging, no details can yet be given. *William McKenzie*

Urogenital System

669. **Salicylamide and Acetylsalicylic Acid in Recurrent Urolithiasis**
E. L. PRIEN and B. S. WALKER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160** 355–360, Feb. 4, 1956. 18 refs.

Writing from Boston University School of Medicine the authors discuss the rate of recurrence of urinary calculi (which they state ranges from 15 to 50%) and also the various regimens which have been used in the attempt to prevent recurrence. They stress the need for careful analysis of the stones and point out that 90% of all urinary calculi in North America are calcium-containing. Glucuronides are known to increase the solubility of calcium phosphate, and although glucuronides are present normally in small amounts in urine, their excretion can be markedly increased by administering compounds that conjugate with glucuronic acid.

On this basis they have treated 19 patients with urinary calculi with 2 g. of acetylsalicylic acid or salicylamide daily. In 17 out of 19 cases followed up for 18 to 24 months there was no recurrence of stone or increase in the size of the existing calculi. In the remaining 2 cases there was increase in the size of the stone in one and recurrences continued in the other. They [rightly] conclude that the administration of salicylates in such cases seems to offer a promising but unproved form of therapy.

Roland N. Jones

670. **Bilateral and Recurrent Renal Calculi. Evidence Indicating Renal Collagen Abnormality and Results of Salicylate Therapy**
R. BAKER and J. P. CONNELLY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 1106–1110, March 31, 1956. 13 refs.

The incidence of bilateral and recurrent renal calculi was studied in a total of 356 patients seen at Georgetown University and the District of Columbia General Hospitals, Washington, D.C., between 1949 and 1954. In 8% of the patients bilateral renal calculi were present at the first examination. It was also found that in 9% of the patients from whom renal calculi had been removed there was recurrence in the same or in the opposite kidney. Of particular interest was the absence of any evidence of infection in 43% of patients with bilateral and recurrent calculi. Known aetiological factors, such as obstruction, hyperparathyroidism, and systemic diseases necessitating prolonged bed rest, were found in only 20·4% of the cases. It is suggested that renal lithiasis is probably a bilateral disease, a view supported by the finding that recurrences were more frequent in the contralateral than in the ipsilateral kidney. Needle biopsy of the kidneys in a small series of cases revealed alterations of the tubular connective-tissue matrix of both kidneys in patients with unilateral disease. [Details of these changes are not given.] In the authors' view renal calculosis is a connective-tissue collagen disease, and in their experience treatment with acetylsalicylic acid, cortisone, phenylbutazone, and ACTH reduces the recurrence rate of calculi by " nearly 50% ".

G. W. Csonka

671. **Treatment of Nephrosis with Prednisolone**
G. C. ARNEIL. *Lancet* [*Lancet*] **1**, 409–411, April 14, 1956. 2 figs., 9 refs.

Hitherto the various methods of treating nephrosis, such as with cation-exchange resins, artificial infection with malaria, and hormones, have proved of limited value, all of them provoking diuresis on occasion, but failing to reduce the albuminuria consistently. The author, at the Royal Hospital for Sick Children, Glasgow, has therefore tried the effect of prednisolone in 4 cases of nephrosis in all of which the history, and clinical and biochemical findings were typical. The patients were between 2½ and 8½ years old, and all were oedematous. The drug was given in doses up to 60 mg. per day.

In all 4 cases the albuminuria decreased strikingly within 6 days of starting treatment, and within 2 weeks the daily loss of albumin had decreased from 1 to 4 g. to less than 0·25 g. per 100 ml. Albuminuria ceased altogether in 3 cases, but reappeared in one of them 6 weeks after treatment was stopped. In all 4 cases diuresis began within 8 days of starting treatment and lasted from 6 to 8 days, the fluid lost amounting to 26 to 31% of (non-oedematous) body weight. An increase in serum albumin and γ-globulin levels occurred, and there was a return to normal of the blood cholesterol concentration and erythrocyte sedimentation rate.

G. A. Smart

672. **Prolonged Discontinuous Treatment of the Nephrotic Syndrome in Children with ACTH and Cortisone.** (Le traitement discontinu prolongé du syndrome néphrotique de l'enfant par l'ACTH et la cortisone)
R. DEBRÉ, P. ROYER, B. LÉVEQUE, and Z. MINOR. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 263–275, Jan. 22, 1956. 11 figs., 12 refs.

The authors have treated 10 children with the nephrotic syndrome at the Clinique Médicale des Enfants, Paris, by giving large doses of ACTH or cortisone intermittently over a long period of time. The results were excellent, although the series was not large enough to prove the superiority of this over other types of hormone therapy. Treatment was divided into three periods: (1) a period of 10 days during which ACTH was given in doses of 100 mg. a day; (2) then 100 mg. of ACTH or 300 mg. of cortisone was given 4 days a week until a remission was obtained—if this had not occurred by the end of one month the doses were increased; (3) a maintenance period with similar doses of ACTH or cortisone for 3 days a week for a total of 6 to 12 months.

G. A. Smart

Endocrinology

673. **Maternal Hyperparathyroidism and Parathyroid Deficiency in the Child**
J. BRUCE and J. A. STRONG. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **24**, 307–319, Oct., 1955 [received Jan., 1956]. 3 figs., 26 refs.

In 1954 Mitchell (*Arch. Dis. Childh.*, **29**, 349) reported the case of a child who had shown signs of hypoparathyroidism from his first year. The present authors now describe, from the Western General Hospital, Edinburgh, the case of the mother of this child, who was found to be suffering from hyperparathyroidism due to a parathyroid tumour; it is stated to be the first time that this association has been recorded. The mother's tumour, which weighed 7·8 g., was removed and 1·1 g. of it was inserted into the marrow cavity of the child's left tibia and 2·3 g. implanted into the left rectus abdominis muscle.

As a result of the operation the mother made a steady recovery: the thirst and polyuria ceased, the serum calcium level returned to normal, and osteoporosis disappeared, but the nephrocalcinosis was unchanged. The child developed temporary but profound hypercalcaemia, the serum calcium content rising to 16 mg. per 100 ml. However, by the end of 5 weeks all activity of the implant had ceased, the serum calcium level fell to 8·5 mg. per 100 ml., and treatment with vitamin D had to be resumed. The metabolic effects of the operation on both mother and child are described in detail, and the literature relating to attempts at parathyroid implantation is reviewed. *C. L. Cope*

THYROID GLAND

674. **Thyroid Disorders due to Cranial Trauma.** (Les dysthyroïdies des traumatisés craniens)
R. LAFON, P. PAGES, R. LABAUGE, and A. PAGES. *Revue neurologique* [*Rev. neurol.* (*Paris*)] **93**, 805–816, Dec., 1955 [received April, 1956]. 3 figs., 18 refs.

The authors have studied the effects of cranial trauma on thyroid function in 63 unselected cases of head injury at the Clinic for Mental and Nervous Diseases of the Montpellier Faculty of Medicine. In 3 cases a clinically obvious thyroid disturbance—hyperthyroidism in 2 cases and myxoedema in one—had developed since the injury, and in 47 others some evidence of thyroid dysfunction was found on measuring the uptake of radioactive iodine (^{131}I) by the gland; in 39 cases this indicated hyperfunction and in 8 hypofunction. The thyroid disturbance was sometimes apparently permanent, sometimes only transitory. Hyperthyroidism following cranial trauma probably has an emotional basis in the majority of cases. Administration of thyrotrophic hormone to those patients with evidence of hypothyroidism resulted in a return to normal function, suggesting that the disturbance had a pituitary origin; moreover, in the patient who developed overt myxoedema (a very rare result of trauma) the appearances on cisternography suggested atrophy of the anterior lobe of the gland. This patient had suffered a severe injury after which she was in a coma for 12 days; she was much improved by thyroid treatment. *G. S. Crockett*

675. **Subacute Non-suppurative Thyroiditis. Treatment with Cortisone and Corticotrophin**
G. IZAK and Y. STEIN. *Lancet* [*Lancet*] **1**, 225–226, Feb. 4, 1956. 12 refs.

In this paper from the Rothschild Hadassah-University Hospital, Jerusalem, 5 cases of subacute non-suppurative thyroiditis treated with either corticotrophin or cortisone are reported. In all cases the condition was diagnosed clinically. The patients, females aged 35 to 64, complained of sharp pain in the lower anterior part of the neck which was aggravated by swallowing. There had been intermittent pyrexia for 2 to 6 weeks before admission. On physical examination all the patients appeared seriously ill and were apprehensive and sweating profusely; the pulse rate was high. A fine tremor of the fingers was observed and in all cases there was a diffuse moderate enlargement of the thyroid, which was exquisitely tender and firm. The erythrocyte sedimentation rate was increased and there was leucocytosis. The basal metabolic rate was raised in all cases but the uptake of radioactive iodine was decreased. Within 24 hours of administration of cortisone or corticotrophin a dramatic response was observed, temperature became normal, pain subsided, and the general condition improved considerably. Treatment was continued, the dosage being decreased, for 4 weeks. No immediate or late relapses were observed in the 3 patients treated with cortisone; in 2 given corticotrophin there were mild relapses, which were controlled by an increased dose of the drug. No late recurrences were observed and none of the patients subsequently developed myxoedema. *G. A. Smart*

676. **Treatment of Hypothyroidism. A Note on the Use of Cortisone**
V. K. SUMMERS. *British Medical Journal* [*Brit. med. J.*] **1**, 430–431, Feb. 25, 1956. 3 refs.

The effect of cortisone therapy in 5 cases of myxoedema is discussed in this paper from Walton Hospital, Liverpool. In all cases the typical clinical manifestations of myxoedema were present and the diagnosis was confirmed by the results of radioactive-iodine studies. The patients (2 males and 3 females) received a standard course of treatment consisting of 25 mg. of cortisone by mouth daily for 28 days. Within 48 hours of the start of treatment a remarkable change was observed, the patients showing increased mental and physical activity

in contrast to their previous apathy. Axillary sweating was noticeable within 4 or 5 days. There was no change in the facial appearance, and no significant change was observed in the serum concentrations of sodium, potassium, and chloride. Hypoglycaemic unresponsiveness, which was present in all cases, was unaffected by the treatment. The blood picture was unchanged. In 2 cases there was a rise in serum cholesterol level. The Kepler water diuresis test in 4 cases before treatment gave mean values of 2·1, 2·1; 2·3,and 3 ml. per minute respectively; after treatment the average water excretion was 3, 3·5, 4·5, and 6 ml. per minute respectively. The 17-ketosteroid excretion rose in all cases after administration of cortisone.

The author suggests that quickening of the mental processes is the sole result of cortisone therapy in hypothyroidism. In one case in the series there was reactivation of rheumatoid arthritis.

I. McLean Baird

677. **Perceptive Deafness in Hypothyroidism**
A. E. HOWARTH and H. E. D. LLOYD. *British Medical Journal* [*Brit. med. J.*] **1**, 431–433, Feb. 25, 1956. 10 refs.

In this paper from the Middlesex Hospital, London, 7 cases of hypothyroidism associated with deafness are described. The basal metabolic rate, which was determined in all cases for confirmation of the diagnosis of hypothyroidism, ranged from −23% to −33%. In one case fragilitas ossium was an associated condition. Perceptive deafness was present in 5 cases and mixed conductive and perceptive deafness, as revealed by the response to the Rinne test and the audiogram, in 2. With thyroid medication perceptive deafness improved in one case, slightly in 2 cases, and was unchanged in 2; mixed deafness improved markedly in one case but did not respond in the other. *I. McLean Baird*

678. **Plasma Activity Levels in Radio-iodine Tests of Thyroid Function**
H. A. HUGHES and R. M. MILLER. *British Medical Journal* [*Brit. med. J.*] **1**, 493–494, March 3, 1956. 7 refs.

Using radioactive iodine (^{131}I), the authors have investigated the thyroid function of 80 patients living in south-east England, the 48-hour total plasma radioactivity being used as the most practicable routine test. In addition, the ratio of total plasma activity at 48 hours to that at 2 hours, the " T " index of Fraser *et al.* (*Quart. J. Med.*, 1953, **22**, 99; *Abstracts of World Medicine*, 1953, **14**, 232), and the 24-hour urinary excretion of ^{131}I were determined in a limited number of cases. The patients were divided into 3 groups: (1) 10 with marked hyperthyroidism—5 with severe toxic goitre and 5 with severe exophthalmic Graves's disease; (2) an intermediate group of 20, 11 with mild toxic goitre and 9 with mild exophthalmic Graves's disease; and (3) 50 patients with suspected hyperthyroidism but subsequently judged on clinical grounds to have normal thyroid function. The basal metabolic rate was determined in some cases, using the standard method of Benedict and Roth.

The 48-hour total plasma activity was found to give reliable results in the diagnosis of hyperthyroidism. For example, the probabilities that total plasma activity can exceed 0·4 and 0·5% per litre in normal subjects ar onlye 3·5% and 0·6% respectively. Thus, a value of 0·4% or less almost certainly indicates normal thyroid function; values of less than 0·7% per litre are unlikely to occur in thyrotoxicosis. The sensitivity of the test is such that an accurate assessment of thyroid function cannot be obtained in borderline cases, but there is evidence that a gradation of 48-hour plasma activity exists throughout the intermediate group. The authors point out that these results are in good agreement with those of other workers and conclude that determination of the 48-hour total plasma radioactivity is a useful and reliable test of thyroid function. *Norval Taylor*

679. **Clinical Application of an Assay of Thyroid-stimulating Hormone in Relation to Exophthalmos**
I. C. GILLILAND and J. I. STRUDWICK. *British Medical Journal* [*Brit. med. J.*] **1**, 378–381, Feb. 18, 1956. 23 refs.

The authors, at the Postgraduate Medical School of London, attempted to assess the amount of thyroid stimulating hormone (T.S.H.) present in the serum of a number of patients suffering from various thyroid disorders, the method used being based on the release by the hormone of ^{131}I from the thyroid of day-old chicks. Endogenous T.S.H. activity was suppressed by administration of 8 μg. of L-thyroxine daily. Control assays were carried out with T.S.H. of known potency. In sera from 5 healthy subjects T.S.H. activity was either undetectable or was very low; likewise there was little or no response in serum from 3 patients with Simmonds's disease. In myxoedema the results varied, but in 2 patients with myxoedema following thyroidectomy and in 2 young cretins the serum level of T.S.H. was high; however, no T.S.H. activity could be detected in the serum of one of these cretins after thyroid therapy for 6 weeks. In 17 cases of thyrotoxicosis the serum level of T.S.H. varied widely; it was increased in 8 patients with severe eye signs. On the other hand in 3 patients with marked exophthalmos but without thyrotoxicosis the serum T.S.H. activity was similar to that observed in healthy subjects.

The authors conclude that some pituitary factor other than T.S.H. is the cause of the exophthalmos.

D. G. Adamson

680. **The Functional State of the Adrenal Cortex in Thyrotoxic Patients.** (Функциональное состояние коры надпочечников у больных тиреотоксикозом)
E. Z. GINCHERMAN. *Проблемы Эндокринологии и Гортонотерапии* [*Probl. Endokr. Gormonoter.*] **2**, 23–30, No. 2, March–April, 1956. 2 figs., 20 refs.

At the All-Union Institute of Experimental Endocrinology, Moscow, adrenocortical function was assessed in 63 goitrous patients, 9 of whom were euthyroid and 54 thyrotoxic (29 severely, 22 moderately, and 3 mildly), primarily by means of the standard Kepler water excretion test. The excretion factor was less than 25, indicating impairment of adrenocortical function, in 26 of the 29 patients with severe thyrotoxicosis and in 10 of the 22 with moderate thyrotoxicosis, returning to normal

in 64% after thyroidectomy. It was above that level in all the remaining patients and in 8 normal control subjects. Of those patients in whom the excretion factor was below 25, 85% had a relative lymphocytosis of over 30%: in one case 10 injections of cortical extract reduced this figure from 46 to 35%. The average diastolic blood pressure of patients in this group was 64 mm. Hg and the pulse pressure 70 mm. Hg (the corresponding values for euthyroid control subjects being 72 and 43 to 48 mm. Hg respectively), their muscle power as measured by dynamometer was below normal, and there was some pigmentation of the mucous membranes. The daily urinary excretion of neutral 17-ketosteroids measured in 12 women chosen from this group varied from 4 to 10·8 mg. (normal 7 to 14 mg.).

The author suggests that these observations point to the presence of adrenocortical hypofunction in a significant proportion of cases of severe or moderately severe thyrotoxicosis. In patients with severe thyrotoxicosis of less than 10 months' duration or with moderate thyrotoxicosis of less than 2 years' duration, however, the result of Kepler's test was normal. The urinary uric-acid : creatinine ratio averaged 0·6 (normal 0·3 to 0·4) in 80% of a group of 20 such cases, while the 17-ketosteroid excretion was not less than 17 mg. in 24 hours in 5 women from this group. These results suggest to the author the presence of adrenocortical overactivity, and he consequently postulates that in thyrotoxicosis initial overactivity of the adrenal cortex is followed by its hypofunction. He concludes that there may be room for the use of adrenal cortical extract, deoxycortone, and cortisone in the treatment of thyrotoxicosis.

Marcel Malden

ADRENAL GLANDS

681. **Phaeochromocytoma: Phentolamine (Rogitine) as a Diagnostic Screening Agent in Sustained Hypertension**
G. SHAW. *Scottish Medical Journal* [*Scot. med. J.*] 1, 89–96, March, 1956. 3 figs., 19 refs.

This report from the Southern General Hospital, Glasgow, describes the results of administering phentolamine (" rogitine ") to patients suffering from essential hypertension of moderate to severe degree with a view to detecting those in whom it was due to phaeochromocytoma. Injections of 5 mg. of the drug (46 intravenous, 19 intramuscular) were given on 65 occasions to 59 patients. When 5 mg. of phentolamine was injected intravenously in 2 cases of proven phaeochromocytoma during a paroxysm of hypertension, spontaneous in one case and induced by histamine (0·01 mg. intravenously) in the other, there was an immediate and dramatic fall of the systolic and diastolic pressures by 80 to 100 mm. Hg, associated with relief of symptoms, in both cases.

For the purposes of the test the intravenous route was found to be more reliable than the intramuscular, false negative results being sometimes obtained with the latter. On the other hand the intravenous test gave rise to some difficulties in interpretation owing to the high proportion of cases (about 90%) in which a fall of pressure by 20 to 30 mm. Hg may occur. When the limits of 35 and 25 mm. Hg were accepted as the maximum falls in systolic and diastolic pressure respectively to be expected in cases of hypertensive vascular disease 8 false positive results were obtained, due variously to raised blood urea level, low initial pressure, or some unexplained depressor action of the drug. In 6 of these 8 cases urinary catechol excretion was normal (less than 80 μg. a day).

No serious side-effects of phentolamine administration were noted in the group tested. Feelings of warmth, palpitation, or light-headedness were reported by about one-third of the patients, due possibly to the increased pulse rate.

It would seem that although phentolamine is a useful screening agent for phaeochromocytoma, the test is not sufficiently reliable to be used alone, the occurrence of equivocal and false positive results making necessary additional investigations, preferably the assay of urinary catechol output. So far, false positive results with the latter test have not been encountered. *G. B. West*

682. **Effect of New Adrenal Steroids on Electrolyte and Water Excretion**
J. J. CHART, N. HETZEL, and R. GAUNT. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. (N.Y.)*] **91**, 73–75, Jan., 1956. 1 fig., 10 refs.

An experimental investigation is reported of the effects of prednisone, prednisolone, hydrocortisone, and of deoxycortone (DC) on the excretion of water, sodium, and potassium in adrenalectomized male rats. The animals received by stomach tube 18 hours after adrenalectomy 3 ml. of distilled water per 100 sq. cm. body surface; this was repeated one hour later. The rate of water excretion was studied at half-hourly intervals for 5 hours and the total amounts of sodium and potassium excreted were estimated by flame photometry. The effect of treatment was expressed in a single figure, the " index of diuresis ", which was determined by the method of Kreiger and Kilvington as used by Ham and Landis (*J. clin. Invest.*, 1942, **21**, 455). Steroids were administered in oil, either in solution or partial suspension, in a dosage per rat of 0·1 to 5 mg., one-half of the total dose being injected subcutaneously at the time of adrenalectomy and the other half 30 minutes before the first water load. Control animals received sesame oil.

All the steroids tested enhanced water and potassium excretion; prednisone, prednisolone, and hydrocortisone were equally potent, DC being less effective. DC caused sodium retention, but the other three steroids were equally active in enhancing sodium excretion.

D. G. Adamson

683. **The Acute Renal Effects of 9-Alpha Fluorohydrocortisone in Human Subjects with Intact Adrenals**
E. R. HUFFMAN, G. M. WILSON, G. M. CLARK, and C. J. SMYTH. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **47**, 747–751, May, 1956. 13 refs.

684. **Pathophysiology and Treatment of Adrenal Crisis**
M. B. LIPSETT and O. H. PEARSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 511–514, March 15, 1956. 3 figs., 24 refs.

The clinical condition of adrenal crisis, as seen in bilaterally adrenalectomized patients deprived of cortisone, can be divided into two distinct syndromes: that of sodium loss and that due to deficiency of 17-hydroxycorticosteroids. Previously, sodium depletion was thought to be pre-eminent in patients with Addison's disease, and the usual treatment was with salt and deoxycortone acetate (DCA), although it was recognized that patients could die in adrenal crises even though sodium balance was maintained and serum electrolyte values were normal. Since bilateral adrenalectomy has been undertaken in human subjects the need for cortisone to maintain life has been recognized; this is in contrast to what obtains in adrenalectomized laboratory animals, which can be kept in reasonably good health with salt and DCA administration only. In many cases of adrenal insufficiency or of subtotal adrenalectomy the patient remains in good health without cortisone treatment; it is only when adrenal tissue is completely absent that the dependence on 17-hydroxycorticosteroids becomes apparent.

The authors, from the Sloan–Kettering Institute for Cancer Research and Memorial Center for Cancer and Allied Diseases, New York, present two studies of sodium balance in adrenalectomized patients from whom cortisone treatment had been withdrawn. Adequate sodium intake was ensured and positive sodium balance was maintained throughout the period of cortisone withdrawal, but the clinical condition of the patients deteriorated, and within 3 or 4 days adrenal crisis began to develop. Administration of cortisone quickly reversed the clinical picture. *Nancy Gough*

685. **Cushing's Syndrome and its Response to Adrenalectomy.** (In English)
B. SKANSE, K. GYDELL, H. B. WULFF, and F. KOCH. *Acta medica Scandinavica* [*Acta med. scand.*] **154**, 119–134, March 26, 1956. 2 figs., 24 refs.

Subtotal adrenalectomy was carried out at the General Hospital, Malmö, Sweden, on 7 patients (2 men and 5 women) with Cushing's syndrome. The surgical technique is discussed, the authors expressing their preference for the retroperitoneal approach, although this does not permit both glands to be exposed at once. They advise total resection on one side and a subtotal resection on the other, since this limits the extent of subsequent operation in the event of recurrence. In one of the cases in the series subtotal adrenalectomy was followed by partial remission; later, total adrenalectomy had to be performed for a relapse. One patient died from wound sepsis and renal failure. The authors emphasize that administration of cortisone before and after operation has lessened the risks of surgical treatment. In the remaining 5 patients there was complete remission, symptoms abating over periods of 6 months to one year or longer. In 4 cases microscopical examination revealed normal adrenal tissue. The mental state of the patients improved markedly after operation. In one case diabetes cleared up after adrenalectomy and in another, in which growth had been inhibited, there was an increase in height within less than 12 months. The eosinophil count and the urinary excretion of 11-oxycorticosteroids were the most informative laboratory determinations. *G. S. Crockett*

DIABETES MELLITUS

686. **Diabetic Coma: the Value of a Simple Test for Acetone in the Plasma—an Aid to Diagnosis and Treatment**
C. T. LEE and G. G. DUNCAN. *Metabolism* [*Metabolism*] **5**, 144–149, March, 1956. 16 refs.

The value of estimation of the ketone content of the plasma as a guide in treating diabetic coma is discussed. The level can be determined quite simply by making use of the Rothera reaction as performed with "acetest" tablet reagents, serial dilutions of plasma being applied directly to the tablets. Three cases treated at the Pennsylvania Hospital, Philadelphia, are quoted in which it is claimed that estimation of the ketone content of the plasma was of value. The presence of a high degree of ketonuria may give a misleading idea of the amount of ketones in the blood and lead to overdosage with insulin. The degree of ketonaemia provides a much more accurate guide to treatment and prognosis.
C. L. Cope

687. **Survival of Diabetic Patients after Myocardial Infarction**
R. F. BRADLEY and J. W. BRYFOGLE. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 207–216, Feb., 1956. Bibliography.

Coronary arterial disease is the chief cause of death in diabetics. Among 102 diabetic patients (45 males and 57 females, average age 63 years) admitted to the New England Deaconess Hospital, Boston, with acute myocardial infarction between 1943 and 1948 the "acute" mortality rate was high, 62 (24 males and 38 females) dying within 60 days of the onset of symptoms. Of the total number of patients, 84 died within 5 years. All of 11 patients showing marked hyperglycaemia and acidosis during the course of the acute myocardial infarction died early, 5 of them within 24 hours of the onset of symptoms. *W. J. H. Butterfield*

688. **Acute Pancreatitis Complicating Diabetes Mellitus**
E. T. BOSSAK and R. H. JOELSON. *A.M.A. Archives of Internal Medicine* [*A.M.A. Arch. intern. Med.*] **97**, 201–207, Feb., 1956. 21 refs.

That permanent diabetes may follow acute or recurrent pancreatitis is well established, but the authors suggest that the occurrence of pancreatitis in known diabetics has received insufficient attention. In a review of the records of the Mount Sinai Hospital, New York, from 1936 to 1954 they found that acute pancreatitis had been diagnosed on clinical grounds or at necropsy, or both, in 106 cases. Eight of these patients were previously

known diabetics and their case histories are given in detail. The mortality amongst them was high (6 out of 8) compared with the non-diabetics (24 out of 98), and in none of the fatal cases was pancreatitis diagnosed during life.

The authors discuss the aetiology of the condition, and recommend that acute pancreatitis should be suspected in all cases of diabetic coma resistant to therapy in which there is abdominal pain or tenderness, shock, or oliguria. *P. Hugh-Jones*

689. **Diabetic Pneumaturia**

R. D. Foord, J. D. N. Nabarro, and E. W. Riches. *British Medical Journal* [*Brit. med. J.*] **1**, 433–434, Feb. 25, 1956. 3 figs., 4 refs.

The authors describe 2 cases of diabetic pneumaturia seen at the Middlesex Hospital, London. One patient, an elderly, obese, diabetic woman aged 67, complained of colicky abdominal pain and of passing gas per urethram, the latter being the chief complaint. At laparotomy there was no evidence of a fistula into the bladder. A urinary infection due to *Escherichia coli* was successfully treated by administration of sulphadimidine and the pneumaturia cleared up. Subsequently both the coliform infection and the pneumaturia recurred; a small daily dose of the sulphonamide was necessary thereafter to prevent further relapse. The second patient, a male diabetic aged 63 years, had a coliform urinary-tract infection and pneumaturia associated with prostatic enlargement and obstruction. Retropubic prostatectomy was performed and recovery was uneventful.

The authors suggest that pneumaturia is probably more common than the literature would appear to indicate. In their view diabetes must always be excluded in a patient with pneumaturia, but to do so it is not sufficient to test the urine for sugar since the latter may be removed completely by bacterial action.

I. McLean Baird

690. **Clinical Use of Sorbitol as a Sweetening Agent in Diabetes Mellitus**

C. R. Shuman, R. L. Kemp, R. Coyne, and M. G. Wohl. *American Journal of Clinical Nutrition* [*Amer. J. clin. Nutr.*] **4**, 61–67, Jan.–Feb., 1956. 26 refs.

This paper reports a clinical experiment carried out at the Philadelphia General and Temple University Hospitals, Philadelphia, which was designed to show whether the administration of sorbitol causes an increase in the blood sugar level and glycosuria in diabetic patients. The trial was conducted on 38 patients with diabetes of varying duration and severity. Each patient was given a measured diet and observed for a preliminary period, during which blood glucose determinations were made. Sorbitol was then given in addition to the fixed diet, and the blood glucose determinations were repeated. The sorbitol was given in a "low-fat ice cream" in which it replaced sucrose as the sweetening agent, the daily intake of sorbitol being 36 to 54 g.

There was no change in the blood sugar level during the administration of sorbitol in 5 cases of mild diabetes treated by diet without insulin and no significant change in blood sugar level or insulin requirement in the majority of cases treated with insulin. In only one instance was there a significant rise in blood sugar level following the ingestion of sorbitol, and that was in a patient with advanced hepatic cirrhosis. Further observations, given in an addendum to the paper, confirm that sorbitol can be given to patients whose diabetes is under control without influencing the blood sugar level, but indicate that it may aggravate hyperglycaemia in patients with uncontrolled diabetes. *K. O. Black*

691. **Indications for and Results of the Treatment of Diabetes Mellitus with a Sulphonylurea Derivative Given by Mouth.** (Indikationen und Erfolge der peroralen Behandlung des Diabetes mellitus mit einem Sulfonylharnstoffderivat)

F. Bertram, E. Bendfeldt, and H. Otto. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **81**, 274–278, Feb. 24, 1956. 2 figs., 15 refs.

During the past 10 months 335 diabetics have been treated at the Barmbek General Hospital, Hamburg, with the sulphonamide derivative "BZ 55" (N_1-sulphanilyl-N_2-*n*-butylcarbamide). In their previous paper (*Dtsch. med. Wschr.*, 1955, **80**, 1455; *Abstracts of World Medicine*, 1956, **19**, 385) the authors had expressed the opinion that the age of the patient and the duration of his diabetes were the factors upon which the success of the new drug depended. Now it appears that it is the patient's constitutional pattern which makes or mars the treatment. At one end of the scale is the hypotensive, asthenic, leptosomatic diabetic (*diabète maigre*, insulin deficiency type) to whom insulin is essential and its withdrawal may be dangerous; diabetics of this group, often young people, do not seem to respond well if the new drug is used by itself though it appears to have a place as an adjuvant in combination with reduced doses of insulin. At the other end of the scale is the pyknic, often obese patient, frequently hypertensive if over 45 (*diabète gras*, insulin antagonistic type) who does not always require insulin, in whom a change in the insulin dosage is not as a rule followed by a dangerous reaction, and who rarely becomes comatose; this type of diabetic seems to benefit from the new drug.

In previously untreated cases a loading dosage is given during the first 3 to 4 days (a divided dose of 5 g. daily, reduced by 1 g. each day) followed by 0·5 g. twice daily, along with the customary diet for such cases. Half this dosage may be given in less severe cases. Administration of the drug can often be discontinued after a while [as with insulin in many cases] when the patient will be found to tolerate a greater amount of fat and carbohydrate without glycosuria than before; if administration of the drug has to be resumed subsequently for any reason its effectiveness is the same as originally. In no instance in the authors' series did any resistance to the drug develop.

It is concluded that the results so far are most encouraging, but observation will have to be continued for a longer period before the final judgment can be pronounced. *L. H. Worth*

The Rheumatic Diseases

692. **Recent Clinical and Laboratory Observations on the Treatment of Rheumatic Diseases with Prednisone, with Special Reference to Long-term Treatment.** (Ulteriori osservazioni cliniche e di laboratorio sulla cura delle malattie reumatiche con prednisone, con particolare riguardo alle cure protratte)
A. ROBECCHI, V. DANEO, and G. MARRAZZI. *Minerva medica* [*Minerva med. (Torino)*] **47**, 295–305, Feb. 3, 1956. 1 fig.

At the Rheumatological Centre of the City of Turin 137 patients with various rheumatic diseases were treated with prednisone given by mouth for periods ranging from a few days to 8 months. The series included 11 patients with rheumatic fever, 53 with rheumatoid arthritis, 4 with ankylosing spondylitis, 12 with acute gouty arthritis, 17 with osteoarthritis, 36 with periarthritis of the shoulder, and 4 with miscellaneous disorders.

The hormone treatment of each group is described in detail; it was usually combined with and followed by other known methods of treatment. For example, in rheumatic fever the best results were achieved by giving prednisone by mouth in doses up to 50 mg. daily for 4 weeks, followed by ACTH for a few days when the condition had been stabilized, and finally a course of salicylates.

In rheumatoid arthritis the average initial dosage of prednisone was 30 to 40 mg. daily. After satisfactory general improvement had been obtained this was reduced to 5 to 20 mg. daily, which was given for periods up to 8 months.

This treatment was accompanied by general and dietary measures and in some cases by intra-articular injections of hydrocortisone or gold therapy. It is stated that the rapid action of prednisone permits the somewhat delayed effects of gold treatment to act in the most favourable circumstances, while the gold helps to stabilize the excellent, but short-lived, effects of prednisone.

Side-effects were rare and were not severe: irritability, sleeplessness, roundness of the face, and indigestion were the most frequently observed.

V. C. Medvei

693. **Discoid Lupus Erythematosus: An Analysis of Its Systemic Manifestations**
E. L. DUBOIS and S. MARTEL. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 482–496, March, 1956. 18 refs.

In order to demonstrate that systemic changes are common in discoid lupus erythematosus the authors obtained a complete history and carried out physical examinations and laboratory investigations in 41 cases of the disease seen at the Los Angeles County Hospital, California. In 26 cases the discoid lupus was confined to the face, and in 16 of them there was evidence at some time during the illness of arthritis, fever, Raynaud's phenomenon, pleurisy, or other systemic changes. Generalized discoid lupus erythematosus was present in the remaining 15 cases, in 14 of which systemic changes developed. When those cases in which there were leucopenia, an increased erythrocyte sedimentation rate, hyperglobulinaemia, or abnormalities in liver function were also considered, it was found that in 24 of the 26 cases of localized disease and in all 15 cases of generalized disease there was evidence of systemic involvement. In 3 cases the result of the L.E.-cell test was positive 3, 5, and 10 years respectively after the onset of the disease.

The authors consider that the classification of lupus erythematosus is arbitrary and that the so-called discoid form is, from its inception, a systemic disease.

E. G. Rees

694. **Neuritis Associated with Systemic Lupus Erythematosus. A Report of Five Cases, with Necropsy in Two**
A. A. BAILEY, G. P. SAYRE, and E. C. CLARK. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 251–259, March, 1956. 2 figs., 7 refs.

Since 1949 the authors have seen at the Mayo Clinic 5 cases of systemic lupus erythematosus associated with peripheral neuritis. In all the cases the presenting signs and symptoms were diagnostic of lupus erythematosus and on the whole the results of laboratory investigations were confirmatory. The result of the L.E.-cell test was positive in all 5 cases. The neurological manifestations varied in character and intensity, suggesting involvement of peripheral nerves, posterior root ganglia and the posterior column of the spinal cord, and focal cerebral damage with involvement of cranial-nerve nuclei. The protein content of the cerebrospinal fluid was often greatly increased. Clinically, signs and symptoms mimicked those of the Guillain–Barré and the mononeuritis multiplex syndromes. Necropsy was performed in 2 cases; in one the vascular changes suggested periarteritis nodosa, but the usual lesion was intimal thickening. Changes in the central nervous system were scattered, consisting mostly in axis-cylinder degeneration and demyelinization affecting peripheral nerves, posterior root ganglia, and posterior columns. In the authors' opinion it appeared unlikely that the nerve changes described could be accounted for by vascular degeneration alone.

[Experience suggests that the L.E.-cell test is not as specific as was thought. The absence, therefore, of definite vascular lesions to explain these rather bizarre neurological manifestations makes it difficult to accept them as part of the syndrome of systemic lupus erythematosus.] *J. N. Harris-Jones*

RHEUMATIC FEVER

695. **Rheumatic Fever Pneumonitis: a Clinical and Pathologic Study of 35 Cases**
M. J. Lustok and J. F. Kuzma. *Annals of Internal Medicine* [*Ann. intern. Med.*] **44**, 337–357, Feb., 1956. 13 figs., 14 refs.

Pneumonitis was found at necropsy in 35 cases of rheumatic fever terminating fatally and rapidly in the acute phase. It was found that the pneumonitis was not a specific entity, being similar to that found in a number of other diseases. However, the frequency of the condition, which was not diagnosed before death in any of these cases, and the magnitude of the pathological changes are considered to warrant the designation of "rheumatic fever pneumonitis". In all cases rheumatic carditis was present, but the degree and prominence of respiratory distress, cough, chest pain, cyanosis, and haemoptysis were out of proportion to the general condition of the patient and the degree of cardiac involvement. One patient, in whom the condition was suspected ante mortem, was treated with ACTH, with regression of fever, erythrocyte sedimentation rate, and carditis, but the respiratory distress increased to the fatal termination. Death occurred in 15 cases within 3 weeks of the onset of pneumonitis. [The incidence of the condition and the total number of cases of rheumatic fever from which this series is derived are not specified.]

There were no significant laboratory findings. Radiographs of the chest showed increased perivascular markings arising from the hilus and progressing to nodulation, confluence, and massive consolidation with relatively clear apices and bases. The main morbid anatomical findings were: (1) alveolar haemorrhages; (2) alveolar-wall necrosis; (3) hyaline membranes; (4) proliferation of alveolar lining cells; (5) Masson organized bodies; (6) bronchiolar changes; and (7) changes in the blood vessels. These findings are fully and well illustrated and a number of radiographs are reproduced. A useful bibliography is given. *Harry Coke*

696. **The Diagnostic Significance of Plasma Protein Changes in Acute Rheumatic Fever**
R. F. Jacox. *New York State Journal of Medicine* [*N.Y. St. J. Med.*] **56**, 672–679, March 1, 1956. 7 figs., 10 refs.

Quantitative estimation of the inflammatory process is of great importance in rheumatic fever. One of the most widely used methods of assessment is determination of the erythrocyte sedimentation rate (E.S.R.); another, more recent, method is estimation of C-reactive protein in the serum. Both these methods depend on changes taking place in the serum protein components, and in rheumatic fever electrophoretic studies have shown that changes of a quantitative nature do occur. The discovery of the cationic detergent technique has made it possible to make frequent and consecutive determinations of serum protein fractions and to measure accurately the alpha and beta–gamma fractions as well as the albumin and fibrinogen concentrations.

During the past three years the author, at the University of Rochester School of Medicine and Dentistry, New York, has studied some 60 patients with rheumatic fever, and the present paper concerns 6 of these whose serum was examined over a period of time by means of the cationic detergent fractionation technique. It is pointed out that in healthy subjects the plasma protein pattern is remarkably constant. Thus in a healthy man of 26 whose serum proteins were analysed weekly for 6 months albumin concentration varied only from 4·5 to 5·3 g., fibrinogen from 0·3 to 0·45 g., beta–gamma globulin from 1·3 to 2 g., and alpha-globulin content from 0·7 to 1 g. per 100 ml. In all 6 cases of rheumatic fever the serum alpha-globulin and fibrinogen concentrations were found to be significantly elevated and that of albumin depressed during the acute phase of the attack. The degree of change and the duration of the abnormal pattern paralleled the severity and duration of the rheumatic process. The E.S.R. and C-reactive protein concentration tended to return to normal levels before the alpha-globulin fraction as revealed by the cationic detergent technique. The author concludes that cationic detergent fractionation is a more sensitive index of inflammatory activity than the other two methods referred to. *D. Preiskel*

697. **The Comparative Action of Hormones and Salicylates in the Treatment of Acute Articular Rheumatism in Children.** (Traitement du rhumatisme articulaire aigu chez l'enfant. Action comparée du traitement hormonal et du traitement salicylé)
R. A. Marquézy, J. di Matteo, C. Bach, and J. Schrub. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **32**, 1115–1127, March 30, 1956. 16 figs., 11 refs.

The effects of ACTH (corticotrophin), cortisone, and hydrocortisone in the treatment of acute rheumatism in childhood were compared at the Hôpital Trousseau, Paris, 87 patients being treated for 100 attacks, of which 61 were treated with ACTH by injection, 24 with cortisone by mouth, and 15 with hydrocortisone by mouth. The daily dosage of ACTH was 50 to 100 mg., that of cortisone about double this amount, and that of hydrocortisone slightly less. No significant difference was observed between the three types of treatment, the duration of which varied greatly, but except in severe cases or those with carditis a "short" course of treatment lasting 15 to 20 days appeared to be as effective as a longer course. The effect of the hormones was most striking in cases of pericarditis. In children in whom the myocarditis dominated the picture the effect was less marked, and in those in whom endocarditis was predominant the effect was difficult to evaluate.

The results obtained with hormone therapy were compared with those obtained in 128 cases treated previously with sodium salicylate. The temperature and erythrocyte sedimentation rate returned to normal more rapidly on the whole in the hormone-treated cases (though in a small group of cases (18) treated with acetylsalicylic acid the effect on fever and arthritis was comparable with that of cortisone). In some cases treated with hormones, however, after the initial fall in temperature a slight rise

was noted which might persist for several weeks without other signs of progressive disease. The authors distinguish this from the rebound phenomenon, which occurred in about half the cases when treatment was stopped or the dose reduced. It was difficult to compare accurately the effects on the course of the carditis, but 14 of the 128 patients treated with salicylates died within 12 months, compared with only one of the 87 treated with hormones. There was no marked difference in the development and persistence of valvular lesions between the two groups. Hormone therapy did little to reduce the incidence of subsequent relapses, which occurred in about one-third of the cases.

[It should be noted that the two series are not strictly comparable, as they were not treated simultaneously.]

C. Bruce Perry

698. **Prevention of Recurrent Rheumatic Fever: the Use of Repository Benzathine Penicillin G**

A. M. DIEHL, T. R. HAMILTON, and J. S. MAY. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala)*] **49**, 250–259, March, 1956. 3 figs., 17 refs.

With the object of preventing a recurrence of rheumatic fever 118 children suffering from the disease at the Children's Convalescent Center, Kansas City, were each given 1,200,000 units of benzathine penicillin intramuscularly every 28 days for periods varying from 6 to 32 months. Nose and throat swabs were examined just before the injection was given and also during acute respiratory infections with fever or sore throat. When β-haemolytic streptococci were isolated initially a second specimen was cultured within 48 hours of the injection. Throughout the investigation the organisms were grouped according to Lancefield's system. Just before each injection blood was withdrawn for the determination of antistreptolysin-O titre.

Of 79 nose and throat swabs cultured before prophylactic injection, 5 were positive for β-haemolytic streptococci, and of 2,738 cultured afterwards, 49 (1·8%) were positive, the organism in 13 of these belonging to Lancefield Group A. In only 5 instances were the follow-up cultures positive. In one case streptococci persisted for 11 days after the injection, and the prophylactic treatment had to be augmented with injections of procaine penicillin. The antistreptolysin-O titre was determined on 2,546 occasions; a significant rise in titre from previous levels was observed in 7 instances, in 3 of which the rise immediately followed the start of prophylactic treatment and in 4 it occurred several months later. In none of these cases had a positive culture been obtained one or 2 months earlier. In one case a titre of over 500 units persisted for 11 months.

A total of 3,235 injections of penicillin were given without serious complications. An erythematous macular rash developed in 3 patients one to 12 days after the injection, but was only temporary, and one child had polyarthralgia as well. The injections were continued in these 3 cases without further reactions, except for the recurrence of the rash in one. Pain at the site of the injection was common and was occasionally associated with limping.

There was no relapse of rheumatic fever during the period of observation. The authors consider that prophylaxis is more certain with intramuscular injection than with oral administration because adequate blood levels are maintained more continuously and there is no doubt that the patients actually receive the drug prescribed.

John Lorber

699. **The Antistreptolysin-O Titre in Rheumatic Fever in Children Treated with Cortisone and Prednisone.** (Il titolo O-antistreptolisinico nella malattia reumatica dell'infanzia trattata con cortisone e prednisone)

I. LANZA, R. MORBIDELLI, and G. PAPOTTI. *Minerva Medica* [*Minerva med. (Torino)*] **1**, 553–557, Feb. 28, 1956. 1 fig., 33 refs.

The effects of cortisone, in high and in low dosage, and of prednisone on the serum titre of antistreptolysin O in 21 patients aged 5 to 13 years with rheumatic fever were studied at the Ospedale Maria Vittoria, Turin. In addition to hormone therapy, chemotherapy and salicylates were given in some cases; neither of these exerts any influence on the antistreptolysin titre. High-dosage cortisone treatment began with 150 to 200 mg. daily for 3 days, then 125 mg. daily for 5 to 7 days, followed by 75 mg. daily, the total period of treatment being 2 to 6 weeks. For low-dosage cortisone treatment 1 to 3 mg. per kg. body weight was given intramuscularly daily divided into 2 or 3 doses. Prednisone was given in a dosage of 0·5 to 1 mg. per kg. daily by mouth divided into 3 or 4 doses. Low-dosage cortisone and prednisone were given in repeated courses of 15 to 25 days' duration according to clinical requirements. The numbers of patients receiving the three treatments were 3, 10, and 8 respectively.

The antistreptolysin titre was determined before treatment in all cases and again every 8 to 18 days for a total of 40 to 70 days. In the group receiving high-dosage cortisone the titre returned to normal in 30 to 45 days, whereas in the other groups it fell more gradually and slowly, returning to normal in 35 to 70 days. Without hormone treatment the antistreptolysin titre remains elevated for 4 to 6 months.

The initial antistreptolysin titre and the rate of change did not appear to be related to the clinical severity of the disease. The erythrocyte sedimentation rate on the other hand more closely reflects the clinical state, but is not so specific and gives no indication of the level of antibody formation.

F. Hillman

700. **Relationship of Immune Response to Group A Streptococci to the Course of Acute, Chronic and Recurrent Rheumatic Fever**

G. H. STOLLERMAN, A. J. LEWIS, I. SCHULTZ, and A. TARANTA. *American Journal of Medicine* [*Amer. J. Med.*] **20**, 163–169, Feb., 1956. 4 figs., 15 refs.

The authors have attempted to answer the question whether recurrences of rheumatic fever are due to repeated subclinical streptococcal infection by relating the immune response to such infection to the clinical course of the disease. In a series of 580 patients with rheumatic fever at Irvington House Hospital, Irvington-

on-Hudson, New York, cultures of throat swabs were made and serial determinations of titres of antistreptolysin O, antistreptokinase, and antihyaluronidase performed at weekly intervals. During the first year of the study chemotherapy was given only when definite infection was confirmed, but during the last 3 years continuous chemoprophylaxis was administered to all the patients.

Within one month of onset of the disease 19 (95%) of 20 patients showed an antistreptolysin-O titre of over 200 units, and at 2 months 66 out of 88 patients (78%) did so. Antihyaluronidase and antistreptokinase titres showed elevation in a rather smaller percentage of cases, but at 2 months 9·5% of the patients showed elevation of at least one of the antibody titres. The level or the rate of decline of the titre showed no relationship to the severity of disease. There were 461 patients in the series who had experienced only a single attack of rheumatic fever.

In 25 of the cases in which the disease ran a course of more than 6 months the same progressive decline in antibody level was observed as in the more acute cases. When a relapse occurred more than 8 weeks after the withdrawal of antirheumatic treatment with aspirin or cortisone, it was always associated with demonstrable evidence of new streptococcal infection. Isolated cases of chorea or erythema marginatum as late manifestations were not associated with fresh streptococcal episodes in this study.

The authors consider that immunological evidence of antecedent streptococcal infection can be found in every new attack of rheumatic fever. *G. Loewi*

CHRONIC RHEUMATISM

701. **Zoxazolamine (Flexin) in Rheumatic Diseases**
R. T. Smith, K. M. Kron, W. P. Peak, and I. F. Hermann. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 745–748, March 3, 1956. 3 refs.

Zoxazolamine is a muscle relaxant which acts centrally on polysynaptic pathways and has virtually no effect on distal structures. It was tried at the Pennsylvania Hospital, Philadelphia, in 95 cases of rheumatic disease in which painful muscle spasm was a prominent feature, the dosage being 750 to 2,000 mg. daily. The response was excellent in 41 and good in 44 cases, muscle spasm being greatly relieved. Of 16 patients with ankylosing spondylitis, 15 were able to perform exercises, morning stiffness being quickly relieved by the first dose. In other groups of patients, chiefly those with "fibrositis", cervical-root syndrome, and rheumatoid arthritis, there was similar but less marked relief. Toxic reactions were noted in 43 cases, and necessitated discontinuance of treatment in 13. The commonest were disturbances of the gastro-intestinal tract and of equilibrium. In 21 patients toxic effects were eliminated when the dosage was reduced by one-half. Zoxazolamine was also given to 5 patients with little muscle spasm, but they did not appear to benefit.

The authors consider that zoxazolamine, because of its effectiveness in relieving spasm and the mildness and controllability of its side-effects, is the best muscle relaxant they have yet tried. *B. E. W. Mace*

702. **On the Correlation between Biopsy Findings and the Congo Red Test in Rheumatoid Arthritis.** [In English]
E. Sairanen, H. M. Koskinen, and T. Holopainen. *Acta rheumatologica Scandinavica* [*Acta rheum. scand.*] **1**, 262–266, 1956. 7 refs.

In 40 cases of rheumatoid arthritis in which amyloid change had been demonstrated in biopsy specimens, mainly of the skin and synovial membranes, at the Hospital of the Rheumatism Foundation, Heinola, Finland, the authors carried out a modified form of the Bennhold test for amyloidosis. With the patient fasting, 1·5 ml. of a 10% solution of Congo red per 10 kg. body weight was injected intravenously and blood samples taken after 3 and again after 60 minutes, the proportion of the injected dye removed from the blood after 60 minutes being calculated from the results of spectrophotometric examination of these and a blank sample taken before the injection. The mean proportion of Congo red disappearing from the blood in the patients with rheumatoid arthritis was 48%, compared with 33% in 21 healthy adults. Moreover, the figure was above 40% in 24 of the former and in only one of the latter. Although the individual figures in the former group varied widely without relation to the biopsy findings, it is concluded that enough amyloid-like material is present in various tissues in certain cases of rheumatoid arthritis to affect the result of the Congo-red test.

R. E. Tunbridge

703. **Rheumatoid Arthritis in a Population Sample**
J. H. Kellgren and J. S. Lawrence. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 1–11, March, 1956. 4 figs., 18 refs.

The authors have attempted to estimate the incidence of rheumatoid arthritis in Leigh, an industrial town in Lancashire of some 48,000 inhabitants. The population studied was from a 1-in-10 sample of houses in the area, and consisted of 537 subjects in the age group 55–64 who had formed the subject of a previous survey and of whom 481 were available for re-examination. Of this number, 380 (173 men and 207 women) were examined clinically and radiologically. The blood was subjected to the differential sheep erythrocyte agglutination test in 350 cases. The results of all the examinations are tabulated and their significance is discussed. The chief problem which arose was the exact definition of rheumatoid arthritis. Osteoarthritis and osteoporosis are common in this age group and must be differentiated. In 9 out of 10 cases of severe rheumatoid arthritis the clinical findings were confirmed by radiological and/or serological tests. Where the condition was not severe, confirmation was less frequent. Clinically, rheumatoid arthritis of all grades of severity was found twice as frequently among the women as among the men. Prevalence rates varied from 1% in men and 3% in women for severe rheumatoid arthritis to 11% and 27% respec-

tively when all grades of severity were considered. An interesting observation was that 20 individuals had positive radiological and/or serological signs without any clinical symptoms of the disease. *William Hughes*

704. **Results of Long-term Treatment of Rheumatoid Arthritis. An Attempt at a Comparative Evaluation of Cortisone and Corticotrophin Therapy**

R. JORDAL. *Danish Medical Bulletin* [*Dan. med. Bull.*] 3, 24–30, Feb., 1956. 3 figs., 15 refs.

At Frederiksborg County Central Hospital, Hillerød, Denmark, 45 patients with rheumatoid arthritis and 3 patients with ankylosing spondylitis were given long-term treatment with ACTH (corticotrophin) in doses ranging from 3·3 to 20 units daily. At the end of 6 months the results were regarded as satisfactory in 34 cases (73%), but after a further 6 months the proportion had fallen to 56%. Treatment was stopped before the end of the course in 4 cases because a sustained remission was obtained, and in 11 cases because it had ceased to be effective. In 6 others treatment had to be stopped because of serious side-effects.

The author points out that for long-term treatment ACTH has the advantage over cortisone that adrenal involution is avoided, so that the risk of adrenal failure due to stress either during or after treatment is absent. Moreover, a number of the in-patients who stopped the injections abruptly, contrary to instructions, suffered no ill-effects such as are seen on sudden withdrawal of cortisone. He points out, however, that there is some variation in the potency of ACTH from different sources and also from batch to batch from the same source. On the whole he considers that ACTH is preferable to cortisone for long-term treatment, but he emphasizes that the dose should be as small as possible.

Oswald Savage

705. **Kerato-conjunctivitis Sicca and Rheumatoid Arthritis**

M. THOMPSON and S. EADIE. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 21–25, March, 1956. 2 figs., 15 refs.

The authors report a study of Sjögren's syndrome and its complex relationship with rheumatoid arthritis and allied states, carried out at the Northern General Hospital and the Royal Infirmary, Edinburgh. In a previous survey they found that among 210 in-patients with rheumatoid arthritis there was evidence of conjunctivitis sicca in 30. The present paper deals with 18 cases of severe or moderately severe kerato-conjunctivitis, in 14 of which rheumatoid arthritis was present. An additional 16 patients with milder symptoms, all of whom had rheumatoid arthritis, were observed and treated. The original syndrome described by Sjögren comprised three basic clinical features—kerato-conjunctivitis sicca, polyarthritis, and enlarged salivary glands. The limits of the syndrome are difficult to define, partly because diagnosis rests on finding the combination of all three features, and partly because there are many additional features, any number of which may be found in each individual case. Thus of the authors' 18 cases rheumatoid arthritis was noted in 14, laryngo-pharyngo-rhinitis sicca in 12, xerostoma in 14, salivary-gland enlargement in 6, achlorhydria in 5 out of 5 cases examined, and Felty's syndrome in one case. The severity of the ophthalmic condition waxes and wanes and its progress is not related to that of the associated arthritis. In 3 cases corneal ulcer was noted, and in one of these the ulcer perforated, necessitating enucleation of the eye. Treatment is said to be difficult and unsatisfactory. The authors mention systemic administration of cortisone and ACTH, but consider that the value of these hormones is limited. Topical application of cortisone, however, may be of some use. They have had some success in early cases with artificial tears prepared with a gelatin or methylcellulose base. The operation of sealing both lacrimal puncta to conserve tear secretion has been found useful in severe cases. *William Hughes*

706. **Nature of Anaemia in Rheumatoid Arthritis. II. Survival of Transfused Erythrocytes in Patients with Rheumatoid Arthritis**

W. R. M. ALEXANDER, J. RICHMOND, L. M. H. ROY, and J. J. R. DUTHIE. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 12–20, March, 1956. 6 figs., 7 refs.

This paper from the Northern General Hospital, Edinburgh, reports a study of the survival of transfused erythrocytes in 19 patients with active rheumatoid arthritis.

The patients, 3 of whom were male and 16 female, ranged in age between 38 and 75 years. The duration of the disease was from one to 36 years. Normal blood of Group O and suitable Rh group was transfused in the first instance. For the second transfusion (7 cases) blood was taken from donors with rheumatoid arthritis who were all in an active phase of the disease, but only those without severe anaemia—a haemoglobin value not less than 75% of 14·8 g. per 100 ml.—were selected. The mean survival time of normal erythrocytes in the 19 subjects averaged 17·6 days. In the second part of the investigation 7 patients were transfused first from healthy donors and then from donors with rheumatoid arthritis. The average mean survival time of erythrocytes from healthy donors was 16·9 days as against 31·9 days for cells from affected donors. After a second transfusion of cells from a healthy donor the mean survival time increased to 21·9 days, but the difference was not statistically significant. Suppressive doses of ACTH did not alter the mean survival time of transfused cells. The results are illustrated in an interesting series of graphs. It is shown that when blood from healthy donors is transfused there is a rapid initial disappearance of cells followed by a curve approximating to the normal linear mechanism of elimination. In the case of rheumatic donors the shape of the curve approximates the normal. Previous intravenous injections of iron did not alter survival times in 3 patients.

Discussing their results, the authors suggest that increased erythrocyte destruction may be one of the important factors in causing the anaemia of rheumatoid arthritis. *William Hughes*

707. **Clinical Trial of Intravenous and Intramuscular Iron in Rheumatoid Arthritis**
J. B. MILLARD and H. S. BARBER. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 51–54, March, 1956. 9 refs.

The relative values of oral, intravenous, and intramuscular administration of iron in the anaemia of rheumatoid arthritis were studied at the Royal Devonshire Hospital, Buxton, 100 patients being selected according to the haemoglobin level after an initial period of 2 weeks in hospital. The patients were divided into 2 groups and treated as follows: (1) of 50 patients with a haemoglobin level of 10·4 g. per 100 ml. or less, 25 received 300 mg. of ferrous gluconate by mouth 3 times daily for 30 days and 25 received iron intravenously to a total of 1,500 mg. over 8 days; (2) of 50 patients with a mean haemoglobin level of 11·9 g. per 100 ml., 25 were given iron intravenously, also to a total of 1,500 mg. over 8 days, and 25 were given iron intramuscularly to a total dosage calculated by multiplying the haemoglobin deficit by 25 and adding 250 mg.

In the group given iron by mouth the average increase in the haemoglobin level was 6·4%, which remained unaltered during the observation period. In the first group of 25 given iron intravenously there was an average rise of 18·4% at 6 weeks and 24·6% at 10 weeks, while in the second group given iron intravenously the figures were 8·8% and 14·4% respectively. Intramuscular injection of iron resulted in an average rise in the haemoglobin level of 8·2% at 6 weeks and 8·9% at 10 weeks. Thus the view is confirmed that iron by mouth has little effect on the anaemia of rheumatoid arthritis. The authors conclude that although iron by intramuscular injection is more likely to produce a response than iron by mouth, " it is less likely to be effective than the intravenous preparation ". However, the total quantity of iron given by the intramuscular route was less than that given intravenously and this may have accounted for the difference in effect. Since there were no significant reactions to the intramuscular injections it is suggested that larger doses should be tried.

No clear relationship was found between the erythrocyte sedimentation rate and the haemoglobin level; moreover, the authors noted that the best results of parenteral administration of iron were not obtained in patients in whom the erythrocyte sedimentation rate was low initially. *K. C. Robinson*

708. **Spondylitis in Post-pubertal Patients with Rheumatoid Arthritis of Juvenile Onset**
M. ZIFF, V. CONTRERAS, and C. MCEWEN. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 40–45, March, 1956. 4 figs., 6 refs.

Radiographs of the spine and sacro-iliac joints of 16 patients, aged 12 to 50 years, with rheumatoid arthritis which had begun in childhood were examined for evidence of involvement of these joints. In 15 of the 16 there were radiological changes in the spine, in 14 involving the cervical region, where the characteristic lesion was fusion of the apophyseal joint between C2 and C3. In 3 patients there were also features of ankylosing spondylitis with sacro-iliac changes and calcification of the paravertebral ligaments, and in 3 others minor alterations in the sacro-iliac joints without ankylosis. The results of the sheep-cell agglutination test were positive in 13 out of 14 cases. Of a control series of 26 patients in whom rheumatoid arthritis had developed after puberty and had been present for at least 4 years, only one was found to have involvement of the spine on radiological examination.

The authors suggest that the presence of localized cervical spondylitis in a patient with rheumatoid arthritis justifies the assumption that the disease began in childhood. *K. C. Robinson*

709. **The Natural History of Rheumatoid Spondylitis**
B. BLUMBERG and C. RAGAN. *Medicine* [*Medicine (Baltimore)*] **35**, 1–31, Feb., 1956. 10 figs., bibliography.

A detailed account of the natural history of " rheumatoid " [ankylosing] spondylitis is presented, based on a study of those cases in which the diagnosis was made at the Presbyterian Hospital, New York, between 1928 and 1954. The total number of patients concerned was 311, of whom 102 attended for follow-up examination for the purposes of this study, 40 responded to an inquiry by letter, and 14 were reported to be dead, while the remainder could not be traced. Males constituted approximately 80% of the patients; the average age of onset was 27 years.

In evaluating the status of the disease in each case followed up attention was directed to (1) functional ability, (2) pain, (3) physical deformity, (4) *x*-ray changes, and (5) laboratory findings. Functional ability was assessed along the lines suggested by the American Rheumatism Association for rheumatoid arthritis: of 121 patients followed up 2 to 35 years after the onset of the disease, 76% were placed in Class 1, leading " essentially normal occupational lives ", and only 4% in Class 4, leading a " bed and chair existence ". The ability to work was found to be remarkably well maintained, on the average, until the age of 55 years. Severe hip involvement was the cause of poor functional ability in 12 of the 24 cases in Classes 2, 3, and 4, spinal deformity alone being rarely responsible. Pain was greatest in the early, acute phase of the disease and tended to decrease and even to disappear in later years.

The degree of physical deformity of the spine progressed relentlessly with the duration of the disease, though it did not necessarily become very severe. Only 30% of the patients had peripheral joint involvement at the time of examination, although 67% had had such involvement in the past. All the patients examined had a reduced chest expansion, which was less than 0·5 cm. in 60%. There was a history of iritis in 25%. The erythrocyte sedimentation rate was normal in 20% of the patients at the time of examination, but it tended to be elevated in the acute phase of the disease. In only one case was the streptococcal agglutination reaction positive, and there was none in which the Waaler–Rose test gave a positive result. *X*-ray changes in the spinal diarthrodial joints and sacro-iliac joints and paravertebral calcification appeared to proceed unremittingly with the passage of time. *C. E. Quin*

Physical Medicine

710. **The Value of Physiotherapy in Rheumatic Diseases. I. Palliation**

J. S. LAWRENCE and R. J. SLADDEN. *Annals of Physical Medicine* [*Ann. phys. Med.*] **2**, 282–289, Oct., 1955. 2 figs., 8 refs.

An attempt was made at the Walkden Clinic, Manchester, to assess the relative values of eleven different physiotherapeutic procedures in the relief of pain in chronic rheumatic disorders, including short-wave diathermy, ionization, radiant heat, infra-red, ultraviolet, and ultra-sonic irradiation, and wax baths, treatment being followed by massage. Skin and deep-tissue temperatures were determined before and after treatment. The results showed that the greatest relief was obtained with short-wave diathermy but that the effect of histamine ionization was more prolonged. Massage augmented both the degree and duration of the relief.

It is concluded from temperature measurements that short-wave diathermy acts mainly by deep heating, whereas histamine ionization produces its effect by skin stimulation. *Kathleen M. Lawther*

711. **Tissue Temperatures Produced by the Application of Moist Air**

C. E. GOODMAN, A. J. MURPHY, and J. W. RAE. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **37**, 18–22, Jan., 1956. 2 figs., 4 refs.

At the University of Michigan Medical School, Ann Arbor, a study was made in healthy young adult males of the temperature changes in the skin, subcutaneous tissue, muscle, and rectum during and after heating by means of a moist-air cabinet which was heated to 44·4° C. by circulating moist air, this temperature being reached within 10 minutes and then maintained for 30 minutes. Thermocouples were applied to the skin, subcutaneous tissue, and muscle of the anterior aspect of the thigh, and also placed in the rectum, two needle thermocouples being inserted in muscle to depths of 1·5 and 3 cm. respectively, and the temperatures recorded continuously.

A total of 20 experiments were carried out, in which either one leg, both legs, or the entire body below the neck was heated. The results, given in detail, showed that when the entire body was heated the temperatures of skin and subcutaneous tissue rose quickly to averages of 42·3° C. (a rise of 9·7°) and 42·3° C. (a rise of 8·7°) respectively. Muscle was heated slowly, at 1·5 cm. to 39·1° C. (a rise of 4°) and at 3 cm. to 38·2° C. (a rise of 2·4°). The rectal temperature rose to 38·6° C., a rise of 1·2° C. Heating of the entire body produced a greater temperature change than heating both limbs, and the latter was more effective than heating one limb; it was noted that when one limb was heated the opposite limb muscles showed no rise in temperature. After cessation of heating, cooling occurred rapidly in the skin and subcutaneous tissue and gradually in muscle. The patients' discomfort was extreme after 20 minutes of entire-body heating, but there were no severe reactions, although the pulse rate rose to 128 per minute; no untoward reactions were observed during heating of the limbs.

The authors consider that the treatment is both safe and effective. *J. B. Millard*

712. **Interferential Currents and Their Applications.** (Les courants interférentiels et leurs applications)

J. KUPPER. *Acta physiotherapica et rheumatologica Belgica* [*Acta physiother. rheum. belg.*] **10**, 189–197, Sept.–Oct., 1955 [received Feb., 1956]. 3 figs., 2 refs.

The author describes a method of producing a low-frequency current of considerable intensity in structures situated deeply in the body. He applies an alternating current of 4,000 c.p.s. at low voltage up to an intensity of 100 mA by one pair of electrodes and a similar current from a second circuit of slightly different frequency (varying between 3,900 and 4,100 c.p.s.) by an independent pair of electrodes so placed that the area to be treated is in the field of both circuits, a low-frequency current of 0–100 c.p.s. being produced in this common field by interference.

Amongst the numerous conditions which he has treated by this method the author quotes 81 cases of traumatic lesions, in which rapid relief of pain and swelling with speedy increase of movement range and restoration of normal function were obtained, and 15 cases of peripheral arterial insufficiency, in which it is claimed that an increase in the oscillometer index was achieved in one or two cases in addition to relief of paraesthesiae and loss of the sensation of cold in the limb; it is also claimed that venous stasis is ameliorated by this method. In 20 cases of " hepatic insufficiency " similarly treated it is claimed that there was marked subjective improvement and that the blood bilirubin level was reduced, as was the abdominal circumference. Side-effects were noted in the treatment of this condition and in 5 cases radiography revealed gastric ulceration. [It is not stated whether the stomach was investigated before treatment was started.] These side-effects were avoided in subsequent cases by reduction of the current intensity. The effect of the treatment on nerve and muscle tissue is also described.

[No control observations were made. So far as is known, the passage of an electric current through living tissue exerts its effect by the generation of heat, by the depolarization of excitable tissue, and, in the case of constant current, possibly by ionic transfer. It is therefore difficult to understand why this particular technique should have any advantage over any other. No indication of any specific effect of " interferential currents " upon living tissue is given.] *Kenneth Tyler*

Neurology and Neurosurgery

713. **A Certain Reflex Present in Infants during the First Few Months of Life.** (Об одном рефлексе у детей первых месяцев жизни)
P. S. Babkin. *Журнал Невропатологии и Психиатрии* [*Zh. Nevropat. Psikhiat.*] **56**, 22–25, No. 1, 1956. 3 figs., 1 ref.

When both hands of a newborn infant are squeezed as it lies on its back, the mouth opens, while at the same time the head is flexed and the eyes close. If one hand only is squeezed the mouth opening is less marked and the flexion of the head is more towards the side of the stimulus. The reflex cannot be elicited by any form of tactile stimulus or by percussion with the patella hammer, but pressure with the latter on the palm evokes the response in most cases. Of 260 newborn infants studied at the Krasnoyarsk Medical Institute, the reflex was absent in only 4. It is present in premature infants and is more marked in these than in full-term babies, while by the age of 4 months it is practically extinct.

The reflex is unconditioned, inborn, and involves proprioceptive afferent impulses from the hand. The centres which mediate the reflex appear to be in the upper parts of the cervical cord and in the brain-stem. The time of disappearance of this reflex coincides roughly with that of certain other brain-stem reflexes, under the influence of cortical development. Part of the motor response is taken over in new, conditioned reflexes which are forming at this time, such as mouth opening in response to visual perception of an object approaching the mouth.

The author states that this reflex has not previously been described [but there is no indication whether any of the literature other than the Russian has been searched].
Alexander Duddington

714. **Clinical Experience with a New Muscle Relaxant, Zoxazolamine. Preliminary Report**
W. Amols. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 742–745, March 3, 1956. 4 figs., 7 refs.

Electromyography provides a useful objective supplement to the clinical assessment of spasticity, and has been used by the author at the Presbyterian Hospital (Columbia University College of Physicians and Surgeons), New York, in evaluating and comparing the effects of certain relaxant drugs. In patients with torticollis the intravenous injection of mephenesin produced a short-lasting reduction of electrical activity in the affected sternomastoid muscle, and this effect was potentiated by premedication with chlorpromazine by mouth. Mephenesin given orally after chlorpromazine produced a slight lessening of spasticity for 1 to 2 hours, but patients soon became refractory to this combination, and side-effects were troublesome. Zoxazolamine ("flexin", 2-amino-5-chlorobenzoxazole) is said to produce, in animals, flaccidity of the limb muscles without depression of consciousness or respiration, and to have a longer duration of action than mephenesin. The effect of this drug was investigated—alone and in combination with chlorpromazine—on 28 patients with spasticity due to a variety of neurological disorders. Zoxazolamine alone had an insignificant effect, but combined with chlorpromazine it produced a definite reduction of muscle tone in 13 out of 16 patients with spasticity of the limbs secondary to affections of the spinal cord. The effect was uneven, and disappointing in that it was not accompanied by improved voluntary control—on the contrary, there was increased weakness of the affected muscles. It did, however, lessen discomfort and aid physiotherapy, and it proved remarkably free from side-effects.
Ronald Woolmer

715. **Effect of Zoxazolamine (Flexin) in Treatment of Spasticity. Preliminary Report**
M. Rodriguez-Gomez, A. Valdes-Rodriguez, and A. L. Drew. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 752–754, March 3, 1956. 3 refs.

The authors have tried the new antispasmodic drug zoxazolamine ("flexin") [see Abstract 714] in doses of 250 to 500 mg. given by mouth 3 or 4 times a day on 18 patients with spastic paraplegia. In 14 they observed objective signs of improvement. Dizziness was the only side-effect noted, and occurred rarely. In 3 cases each of hemiplegia and Parkinsonism the effect of the drug proved unpredictable. One patient was made worse, another improved, and a third showed no effect except drowsiness.
L. Michaelis

716. **Migration of Spike Foci from One Hemisphere to the Other in Children**
A. Lundervold and M. Skatvedt. *Journal of Pediatrics* [*J. Pediat.*] **48**, 457–464, April, 1956. 6 figs., 2 refs.

717. **Reflex Facilitation of Convulsive Activity.** (Déclenchement réflexe de l'activité convulsive)
G. C. Lairy. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 73–85, Feb., 1956. 6 figs., 25 refs.

The role of afferent stimulation in facilitating "convulsive" discharges, immediate or delayed, in the electroencephalogram (EEG) is discussed in this paper from the Hôpital Henri-Rousselle, Paris, the author taking into account such factors as the topography of the discharge, background activity, and quality of stimulus. When a local reflex "convulsive" discharge appears in the region of a cortical focus, irritative or associated with a lesion, this focus need not necessarily be in the projection area of the afferent stimulus. Non-specific systems are usually brought into play, and local discharges, and

also diffuse reflex discharges (mostly consisting of bursts of spike-and-wave or polyspike-and-wave complexes), may be associated with activation, " disactivation ", and startle reactions, as well as with rhythmic stimulation.

The importance both of the background activity (determined by constitutional factors, functional state, and pathological modifications) and of the quality of the stimulus is stressed. More prolonged or delayed discharges are discussed in terms of the physiological concomitants of " stress reactions " following emotional stimuli, with consequent disequilibrium of the various systems affecting cerebral electrical activity, especially in some epileptic subjects. It would seem that there is a dual mechanism for precipitating reflex discharges, involving specific pathways and the ascending reticular system. *William Cobb*

BRAIN AND MENINGES

718. **Benign Intracranial Hypertension**
P. BRADSHAW. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **19**, 28–41, Feb., 1956. 4 figs., 23 refs.

Cases of increased intracranial pressure with papilloedema but with no space-occupying lesion or other well-defined cause to account for these signs have hitherto been described under such terms as " benign serous meningitis ", " otitic hydrocephalus ", and " pseudotumor cerebri ". The present author, reviewing 42 such cases seen at the Radcliffe Infirmary, Oxford, during the period 1938–54 suggests " benign intracranial hypertension " as the most suitable description of the condition in the absence of a fuller understanding of its pathogenesis. These cases fell into 5 clinical groups associated respectively with: (1) infections of the ear or respiratory tract (26 cases); (2) extracranial venous thrombosis (4 cases); (3) obesity (6 cases); (4) trauma (2 cases); and (5) undetermined (4 cases). Summaries of many of the cases are presented, and the clinical course, symptoms, signs, differential diagnosis, pathogenesis, treatment, and prognosis discussed.

[As ventricular dilatation is not a feature of this condition the frequently employed designation " otitic hydrocephalus " is clearly inappropriate even when there is a history of infection of the ear.] *L. Crome*

719. **The Results and Sequelae of Selective Frontal Surgery.** (Résultats et sequelles de la chirurgie frontale sélective)
J. GACHES and J. LE BEAU. *Annales médico-psychologiques* [*Ann. méd.-psychol.*] **1**, 369–384, March, 1956. 2 refs.

The results of selective prefrontal surgery (topectomy, leucotomy, or lobectomy) in 50 patients who have been under observation for more than 5 years after operation are reported from the Hôpital Lariboisière, Paris. The conditions for which operation was undertaken included epilepsy with personality changes (5 cases), mental defect with hyperactivity, with or without fits (9), psychiatric disorders such as schizophrenia and obsessional and hallucinatory neurosis (18), and intractable pain of organic or psychogenic origin (18).

The result, assessed in relation to the condition for which the operation had been undertaken, was regarded as a complete success in 16 cases, a partial success in 19, a partial failure in 9, and a complete failure in 6. From an analysis of these results the authors conclude that intractable pain remains one of the strongest indications for prefrontal surgery, and that psychopathy is a contraindication. Apart from the latter group, no deterioration of personality was encountered and no patient showed any postoperative diminution in intelligence. Out of 36 patients who were not previously epileptic, 3 developed fits after operation and minor electroencephalographic changes were seen in 5 others. The choice of operation in the various clinical groups is discussed. *J. B. Stanton*

720. **Surgery in Spontaneous Subarachnoid Haemorrhage. Operative Treatment of Aneurysms on the Anterior Cerebral and Anterior Communicating Artery**
V. LOGUE. *British Medical Journal* [*Brit. med. J.*] **1**, 473–479, March 3, 1956. 6 figs., 12 refs.

The author points out that although much is known concerning the natural history of spontaneous subarachnoid haemorrhage from intracranial aneurysms, it is difficult to assess the value of surgical treatment from reports in the literature because of the variety of procedures adopted and the different potentialities for ill of aneurysms in different situations, and particularly because of the wide variations in time interval between the initial haemorrhage and the operation. Many surgeons delay operation for several weeks after the initial haemorrhage in the belief that operation during the first 3 weeks leads to a prohibitive mortality. But although the mortality from a delayed operation may be lower, the longer the patient survives after the initial haemorrhage, the smaller is the risk of a recurrence and the less the need for operation, while many lives will be lost from recurrent bleeding during the period of waiting which might have been saved by an early operation.

In this paper from St. George's and the Maida Vale Hospitals, London, he compares the results of early surgical treatment with those of conservative treatment in a series of cases of subarachnoid haemorrhage in all of which the aneurysm responsible was of the common type arising from the anterior communicating artery at or near its junction with the anterior cerebral arteries. There were 73 patients in the series, 37 being treated surgically and 36 conservatively, the latter group being made up of 20 patients who were considered to be too ill for surgery, 12 patients without symptoms, and 4 with an anomalous circle of Willis which prevented clipping of the anterior cerebral artery. The risks of recurrent haemorrhage are emphasized. Of the patients treated conservatively, 20 had more than one haemorrhage, some having as many as 3, while of those treated surgically, 25 had had more than one haemorrhage before operation. Taking both groups together, of 63 recurrent haemorrhages, 12 occurred in the first week, 16 in the second, 12 in the third or fourth week, 12 in the

second month, and 11 after longer intervals. Thus 63% of the recurrences occurred within 4 weeks and 82% within 8 weeks of the original haemorrhage. Of the patients treated conservatively, 16 (44%) died, but it is pointed out that only one of these died from the initial haemorrhage, whereas in subarachnoid haemorrhage the mortality is generally given as 25 to 30%. In haemorrhage from aneurysms of this type, therefore, there would appear to be a strong case for early surgical treatment.

Cerebral ischaemia due to spasm of the vessels related to the aneurysm, together with the effect on the brain tissue of intracerebral bleeding when it occurs, is mainly responsible for the high mortality of operation carried out in the early stages, further damage to the ischaemic areas from retraction of the brain by the surgeon being unavoidable. However, no procedure at present available appears to bring about relief of the vascular spasm and would in any case give rise to the danger of further haemorrhage, and as the intracerebral haematoma resulting from haemorrhage from aneurysms at this site rarely constitutes a threat to the patient's life, treatment should be directed solely towards preventing a further haemorrhage. Operation should not be undertaken unless the patient shows evidence of a reasonable chance of recovery —the author does not accept comatose patients or those with a severe neurological defect for surgical treatment. Angiography is essential to determine not only the site of the aneurysm, but also the side from which it chiefly fills and the presence of adequate cross-circulation. The anterior cerebral artery from which the aneurysm is best filled is then clipped close to the bifurcation of the internal carotid artery and without disturbing the aneurysm itself. This reduces the blood flow through the sac, but does not cut it off altogether, since the lesion can usually be revealed postoperatively by angiography. The operation cannot be performed when both anterior cerebral arteries originate from a common trunk arising from one or other of the internal carotid arteries.

Among the 37 patients so treated there were 5 operative and 3 later deaths, giving a mortality of 21·5%. Of the 29 survivors, 3 were hemiplegic and one suffered a fatal recurrent haemorrhage, the average duration of the follow-up period being just under 2 years.

J. E. A. O'Connell

721. **Vascular Disturbances in the Brainstem Caused by Supratentorial Lesions.** [In English]
H. W. Stenvers. *Folia psychiatrica, neurologica et neurochirurgica Neerlandica* [*Folia psychiat. (Amst.)*] 59, 1–9, Feb., 1956. 14 figs., 16 refs.

The author has been impressed by the frequency with which haemorrhages in the pons and mid-brain are unexpectedly found at necropsy as complications of supratentorial lesions. In this paper from the University of Amsterdam he describes 4 cases in which such haemorrhages were associated respectively with internal carotid thrombosis (bilateral), a tumour of the septum pellucidum, hypertensive cerebral haemorrhage, and a temporo-occipital glioma. It is suggested that the haemorrhages arise from the fine median perforating arteries and the circumferential branches of the basilar artery, which, being frail vessels, are stretched as a result of pushing down of the brain-stem by tentorial herniation, itself consequent on increased supratentorial pressure.

Hugh Garland

722. **Extradural Haematomata of the Posterior Fossa.** (Les hématomes extra-duraux de la fosse cérébelleuse)
D. Petit-Dutaillis, G. Guiot, B. Pertuiset, and Y. Le Besnerais. *Presse médicale* [*Presse méd.*] 64, 521–524, March 21, 1956. 4 figs., 26 refs.

The authors summarize briefly 6 personal cases of extradural haematoma of the posterior fossa, which they consider to be a rare but not exceptional complication of head injury. They have collected a further 46 cases from the literature and they discuss the clinical aspects of these cases together with their own.

The complication appears to affect the young especially, 41% of the 52 patients being under 15 years of age and a further 33% between 16 and 30. Most of the haematomata were unilateral, those on the left side predominating; only 2 were bilateral. The haematoma was sometimes confined to the posterior fossa and sometimes extended above the tentorium. In a few cases there were two loculi, not in communication, one above and one below the tentorium. The authors therefore consider it important when a supratentorial haematoma is found posteriorly always to make sure that there is no subtentorial extension. In most cases the bleeding was venous in origin, from the sinus or torcular, but in many it was not possible to decide its origin. Plain radiographs of the skull showed a fissured fracture crossing the line of the lateral sinus or torcular in 92% of cases.

According to the form of clinical presentation five types may be distinguished. (1) The complication is fulminating in onset, and within a short time of injury, usually after some initial improvement, consciousness is lost or deteriorates and respiratory difficulties and signs of decerebration appear. Localizing signs are usually absent, and when present are often misleading and suggest a supratentorial site. In most reported cases of this type the patient died before treatment could be instituted, and in many the haematoma was a surprise finding at necropsy. (2) In the acute type the picture develops rather more slowly. Usually localizing signs develop at the same time as deterioration in the level of consciousness but, as in the preceding group, they may be misleading and suggest a supratentorial locus. (3) The subacute type is the most common. After a lucid interval of days or weeks signs of cerebellar disorder, raised intracranial pressure, and contralateral pyramidal disturbance, neck pain, and stiffness develop. Cranial nerves are occasionally involved, especially the seventh and twelfth and the oculomotor nerves. Compression of the brain-stem is indicated by cerebral vomiting, difficulty in swallowing, and disturbance of conjugate gaze. In most cases of this type the diagnosis is clear from the localizing signs. (4) In the chronic variety similar localizing signs appear after a period of weeks or months. There is usually evidence of raised intracranial pressure and in such cases a mistaken diagnosis of

cerebral tumour is often made. (5) The "latent" type is represented by a single case in which the patient collapsed suddenly during operation for another injury and was discovered at necropsy to have a haematoma.

Diagnosis is usually easy in cases of the chronic types, but very difficult in acute cases. The presence of a fracture crossing a sinus is suggestive, as is also the presence of hydrocephalus on ventricular puncture or ventriculography. The most useful and certain method of diagnosis is by cerebral angiography, the medium being followed through into the venous phase when, in the lateral view, a characteristic displacement inwards of the lateral sinus or torcular will be seen. The operative results in the series as a whole were: among 4 cases of Type 1 there were 3 deaths; among 13 of Type 2 there were 4 deaths; and of 23 cases of Types 3 and 4 only 2 were fatal. *Brodie Hughes*

723. **Traumatic Intracerebral Hematoma**

R. L. McLaurin and B. H. McBride. *Annals of Surgery* [*Ann. Surg.*] **143**, 294–305, March, 1956. 5 figs., 9 refs.

Approximately 300 cases of head injury are admitted each year to the Cincinnati General Hospital, and over a period of 6 years 16 cases have been seen in which surgical removal of intracerebral haematoma was followed by recovery. These 16 cases form the basis of the present report.

The ages of the patients ranged from 9 to 65 years; all except 5 were under 50 and 8 were under 40, and the authors consider this age distribution to support the view that arteriosclerosis does not increase susceptibility to traumatic intracerebral haemorrhage. The type of injury seemed unimportant in the production of intracerebral haematomata, and there was no correlation between the site of the impact and that of the haematoma. The haematoma was in the temporal lobe in 12 cases, the frontal lobe in 3, and the parietal lobe in one.

The most common signs necessitating surgical exploration were a change in the level of consciousness and hemiparesis. Each of these occurred in 9 patients, "either separately or simultaneously". Asymmetry of pupillary size and response was noted in only 3 cases; in 2 of these the dilatation was ipsilateral and in one contralateral. These signs, as the authors point out, are those of any intracranial clot, and if surface haematomata are not found further measures should be undertaken to exclude the presence of localized subcortical haemorrhage. As the temporal lobe is the most frequent site it should be inspected, and if an underlying haematoma is not encountered and the patient's condition is critical exploratory needling is justified. Associated extradural and/or subdural haematomata were present in 8 cases in the present series. There was no significant correlation between the size of the intracerebral haematoma and the severity of the clinical signs. The authors emphasize that since the clot is often wholly or partially solid it must be removed by cortical incision under direct vision, and that cannula aspiration is unsuitable.

Of the 16 patients, one died from tuberculosis and another in status epilepticus 6 weeks after operation. The remaining 14 were followed up for periods of 2 months to 6 years; 9 were completely symptom-free, and of the 9 who had hemiplegia before operation, only 4 had slight residual weakness. All, with one possible exception, were free from convulsive seizures.

R. G. Rushworth

724. **Cryptic Arteriovenous and Venous Hamartomas of the Brain**

J. V. Crawford and D. S. Russell. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **19**, 1–11, Feb., 1956. 12 figs., 6 refs.

The authors review the clinical and pathological features of a series of 20 cases of spontaneous cerebral and cerebellar haemorrhage from small hamartomata seen at operation or at necropsy at the London and Chase Farm Hospitals. These lesions were often small, giving rise to no symptoms before the catastrophe, and could easily be overlooked by the surgeon or pathologist. The term "cryptic" is therefore proposed as a suitable designation for this condition. Its clinical features are usually characterized by the unheralded acute onset of symptoms, with delayed or, in some cases, incomplete loss of consciousness.

In the present series, 10 of the lesions were related to the convexity of the cerebral hemispheres, 4 were intracerebral, and 6 cerebellar. Of the 9 patients treated surgically, 7 survived operation. *L. Crome*

725. **Ethopropazine (Parsidol) Hydrochloride in Treatment of Paralysis Agitans. Posology, Method of Administration, and Effects**

L. J. Doshay, K. Constable, and F. J. Agate. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 348–351, Feb. 4, 1956. 2 figs., 12 refs.

The authors present, from the Presbyterian Hospital, New York, the results of a therapeutic trial of ethopropazine hydrochloride ("parsidol", "lysivane") in the treatment of Parkinsonism. Of the 147 cases treated, the disease was classified as postencephalitic in 28%, idiopathic in 34%, and as arteriosclerotic in 38%. The effect of treatment was assessed only as "improved" or "not improved", the authors considering it "undesirable to delineate shades of improvement".

Major tremor was improved in 29 out of 42 patients (69%). Muscular rigidity showed "pronounced improvement" in 38 out of 92 patients (41%). Of 17 patients with insomnia, 11 (65%) were improved; but "practically no improvement" occurred in 6 patients with oculogyric crises. The authors conclude that "the drug has a highly selective action against major tremor such as no other current medicament provides", and is "an outstanding addition to the chemotherapy" of Parkinsonism.

[This report suffers from all the defects inherent in an uncontrolled therapeutic trial, however scrupulous the observations, and its claims are uncritical and over-optimistic. The evaluation of therapy in a chronic malady such as Parkinsonism is notoriously difficult and demands a carefully planned approach.]

P. D. Bedford

Psychiatry

726. **A Psychiatric Study of Attempted Suicide in Persons over Sixty Years of Age**
P. O'Neal, E. Robins, and E. H. Schmidt. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 275–284, March, 1956. 10 refs.

As part of a larger study carried out by the authors at Washington University School of Medicine and the St. Louis City Hospital, 19 patients aged 60 and over who had attempted suicide were interviewed and examined. The attempts were assessed as "serious (genuine)" in 12 cases, and were mostly by violent means. Many patients complained of depressive symptoms, but 11 did not relate them to social, personal, or medical problems; 9 had delusions. Every patient was found to be suffering from psychiatric disorder, initially diagnosed as senile or arteriosclerotic dementia (5), manic–depressive psychosis (9), acute confusional state (1), or chronic alcoholism (2). Nine patients also had severe and disabling physical disease, though only 3 related their suicidal attempt to this. Marital and occupational histories were considered not to differ from the average. Only 3 patients gave loneliness as the reason for their attempt; indeed, 12 had been living with relatives. Comparing this group of elderly people with 90 others below the age of 60 who had attempted suicide, it was found that the younger group contained 39% of men, compared with 74% in the older group. In the younger group no definite diagnosis was reached in 23%, 26% of their attempts were not "genuine", marital and other disturbances were very common, and many came from broken homes. Two of the older patients were successful in committing suicide within one year.

The authors stress that every elderly suicidal patient had readily recognizable psychiatric illness for which hospital treatment would often be effective; 14 of the 19 had the common geriatric disorders, psychotic depression or senile or arteriosclerotic psychosis. Comparison of this with an earlier study reported from Edinburgh (*Brit. med. J.*, 1953, **2**, 1186), the findings of which were strikingly similar, suggests that social, occupational, and ageing factors are rarely the primary cause of suicidal attempts in the elderly. *J. N. Agate*

727. **The Treatment of Delirium Tremens**
L. H. Berman. *Quarterly Journal of Studies on Alcohol* [*Quart. J. Stud. Alcohol*] **17**, 28–34, March, 1956. 1 fig., 18 refs.

An investigation was carried out at the Fairfield State Hospital, Newtown, Connecticut, to determine the relative values of sedation, ACTH, and aureomycin in the treatment of delirium tremens. One group of 9 patients received conventional treatment with sedation, vitamins, and fluids, another group of 9 received ACTH, and a group of 4 received aureomycin. The factors of tremulousness, orientation for place and time, auditory and visual hallucinations, fear, confusion, agitation, anorexia, and coordination were evaluated in each patient 3 times a day, a fourfold scale—normal, slight, moderate, and severe—being used. At the end of 6 days all the patients had achieved the same level of improvement, but this improvement had been more rapid in those given conventional treatment. During the first 3 days the values for each of the factors were better in the sedation group than in either the ACTH- or the aureomycin-treated groups. The difference between the improvement under sedation and that under ACTH was statistically significant.

The author considers these results to indicate that sedation with administration of vitamins should continue to be the treatment of choice for delirium tremens, the expensive hormone treatment being used only if this fails. *E. H. Johnson*

728. **Comparison of Chlorpromazine and Reserpine in Treatment of Schizophrenia. A Study of Four Hundred Cases**
A. A. Kurland. *A.M.A. Archives of Neurology and Psychiatry* [*A.M.A. Arch. Neurol. Psychiat.*] **75**, 510–513, May, 1956. 16 refs.

729. **Clinical Reactions and Tolerance to LSD [Lysergic Acid Diethylamide] in Chronic Schizophrenia**
L. S. Cholden, A. Kurland, and C. Savage. *Journal of Nervous and Mental Disease* [*J. nerv. ment. Dis.*] **122**, 211–221, Sept., 1955 [received April, 1956]. 14 refs.

For an investigation at the National Institute of Mental Health, Bethesda, Maryland, of the response in schizophrenia to lysergic acid diethylamide (LSD) 4 patients under 40 years of age with the chronic form of the disease, who had been in hospital for 15 years and showed a stable symptomatology, were selected. Each was observed for 3 weeks, given a placebo for the next 3 weeks, and then given 100 μg. of LSD daily by intramuscular injection. Marked changes in behaviour, which were assessed on rating scales, were noted about half an hour after the injection; these changes were not so pronounced after the second injection, and ceased completely thereafter, as a result, it is thought, of a rapidly developing tolerance. If an interval of 5 days was allowed to elapse before the injections were resumed this tolerance disappeared; increasing the dosage by 100 μg. daily to a total of 500 μg. in 5 days had no effect. There was a cross-tolerance to other lysergic acid derivatives but not to mescaline, suggesting a physiological rather than a psychological basis for the tolerance. A further 16 patients were given LSD [but the details are incomplete].

In conclusion the authors state that the reactions observed could be grouped as follows: (1) covert—the

change in behaviour being subtle and difficult to detect; (2) intensification—the normal symptomatology being exaggerated; and (3) reversal—the mute becoming garrulous and the withdrawn becoming elated.

L. G. Kiloh

730. **On the Effect of " Suavitil " (Benzilic Acid Diethylaminoethylester Hydrochloride) on the Higher Mental Functions of Normal Subjects.** [In English]
H. K. MUNRO. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **30**, 721–728, 1955. 5 refs.

The extent to which intellectual function is impaired after administration of " suavitil " (benactyzine) in moderate doses was studied at Rigshospitalet, Copenhagen, in 8 young healthy adults (6 males and 2 females) of above average intelligence and education, in whom there were assumed to be no mental anomalies. Tests were carried out during the hour following subcutaneous injection of 4 mg. of benactyzine dissolved in 1 ml. of saline, and in parallel series, A and B. Half of the subjects were tested for the first time after injection of benactyzine and the other half after injection of saline. In order of administration the tests were: (1) Memory Test, in which a logical passage was read 1 to 3 minutes after injection and recalled 25 to 30 minutes later (the Danish Binet and Wechsler Memory Scale, Form 1); (2) Serial Sevens Test, beginning 8 to 11 minutes after the injection; (3) Jigsaw Puzzle Test, starting 10 to 14 minutes following the injection, the subject being asked after each puzzle to assess time spent on it and, 20 to 30 minutes later, to indicate which pictures had been done; (4) Digit Symbol Test, 27 to 39 minutes after injection, a modification of a similar test by Wechsler, scored at 10-second intervals for 4 minutes; (5) Verbal Fluency Test, 32 to 44 minutes after injection, subjects recalling as many words as possible beginning with T or R, scored as in (4); (6) Abstraction Test, 37 to 49 minutes following injection, subjects being asked to find the principle of order in 7 letters and to complete the series, scored at 10-second intervals, no time limit; (7) Rating Scale Test, some 33 symptoms being evaluated on a scale 0, (+), +, or ++. Finally the subjects were required to estimate the duration of the whole session.

The results, which are given in tables, suggest that there was no apparent change after benactyzine in the level of intellectual function as measured by Tests 2, 3, 5, and 6, nor were alterations observed in the speed of functioning under distraction in Tests 3, 4, 5, and 6, in spite of the fact that the subjects complained of poor concentration. No difference was noted between subjects and controls in the recall of logical passages, but the passage was read before the effect of the injection had begun and recalled when symptoms were pronounced. Memory for situations not concerned with learning and ability to assess filled time (Test 3) were impaired; ability to assess empty time, however, did not appear to be affected by the drug.

As regards symptoms in Test 7, the author states that in controls these were more like examination anxiety symptoms, but there was considerable overlap and suggestibility was high. There was some correlation between the number and the type of symptoms in the control tests and those recorded after benactyzine; 2 subjects were strongly influenced by the drug, one was moderately affected, and 5 were mildly affected. The most common symptoms noted were a " general feeling of not being fit ", dizziness, paraesthesiae in the limbs, metallic taste in and dryness of the mouth, drowsiness, accommodation difficulties, and heaviness in the limbs. The symptoms reached a maximum during Tests 3 and 4, and in one or two instances had cleared up at the time of Test 6.

Finally, the author states that although the dose of benactyzine was somewhat higher than that given therapeutically, the effect, if any, on ordinary intellectual functioning was slight, although " some highly-organized functions related to registration of a situation simultaneously with attention to a task " seemed somewhat impaired.

J. C. Kenna

731. **Treatment of Psychoses and Psychoneuroses with a New Sedative " Suavitil " .** [In English]
I. MUNKVAD. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] **30**, 729–739, 1955. 5 refs.

At Rigshospitalet, Copenhagen, " suavitil " (benactyzine) in a dosage of 5 mg. 6 times a day and later 10 mg. 6 times a day was given for one week, followed by a placebo for a week, to 22 psychotics (schizophrenia 14, endogenous depression 4, Huntington's chorea 1, endogenous mania 1, paranoid climacteric psychosis 1, depressive state in mental inferiority 1). No systemic toxic effects were noted during administration of the drug; 3 of the schizophrenics appeared less tense, but in general there was no improvement. One patient with fresh schizophrenic symptoms responded to benactyzine but a relapse occurred when the drug was discontinued; several months later when administration was resumed there was no apparent effect.

To 15 ambulatory psychoneurotics (7 males and 8 females aged 24 to 70 years) in whom the disease appeared to be stationary and in whom previous treatment had had little or no effect benactyzine was given by mouth in an initial dosage of 0·5 mg. 3 times a day, increasing slowly to 1·5 mg. 3 times a day. The duration of treatment varied from 10 days to one year. The diagnoses in these cases included obsessive compulsive disorder, psychoneurotic disorder (mixed type), and neurotic depressive reaction. There was improvement in the clinical state in 10 of the 15 cases, this being slight in one, moderate in 6, and marked in 4. The drug was without effect in 4 cases, while the condition of one patient deteriorated. The effective dose appeared to be 3 to 4·5 mg. daily. None of the patients was completely free from symptoms, but some, especially those with obsessions or psychosomatic symptoms, declared spontaneously that they were not troubled as much as before. There was no analgesic or euphoric effect, nor were there any signs of addiction. The author states that the effective duration of the response to this treatment is still open to question.

J. C. Kenna

Dermatology

732. **Eccrine Spiradenoma**

D. W. KERSTING and E. B. HELWIG. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] **73**, 199–227, March, 1956. 6 figs., bibliography.

Writing from the U.S. Armed Forces Institute of Pathology, Washington, D.C., the authors discuss and briefly describe the benign tumours of human sweat glands, of which they distinguish six different types. In the present investigation they have particularly studied the type designated eccrine spiradenoma, of which 136 specimens occurring in 134 patients were available, 2 of the patients (both women) having two tumours each. Of the 134 cases in which the site was known the tumour was on the ventral aspect of the body in 106 (79%), 102 (76%) of them being in the upper half of the body or on the arms. The size ranged from 0·2 to 5 cm. in diameter. Pain or tenderness was noted in 91% of the cases. The clinical appearance was not characteristic, and the diagnosis could be made only histopathologically. In general structure the lesion was seen to be an encapsulated solid tumour surrounded by normal eccrine sweat glands and their ducts and small nerve trunks; the microscopical appearance is described and portrayed in a number of photomicrographs. In all cases the tumour was benign and grew slowly. Clinically, it had to be distinguished from other painful cutaneous tumours such as leiomyoma, glomus tumour, neuroma, and angiolipoma. Local surgical excision, if complete, was curative. The tumour was shown to be derived from eccrine sweat glands. *E. Lipman Cohen*

733. **The Treatment of Plantar Warts**

C. W. MONROE. *Plastic and Reconstructive Surgery* [*Plast. reconstr. Surg.*] **17**, 168–183, Feb., 1956. 9 figs., 9 refs.

The author reviews 72 consecutive cases of plantar warts treated privately over a period of 9 years. He considers that small, painless warts up to 5 mm. in diameter do not require treatment because as a rule they disappear spontaneously after about 6 months. For larger warts and those causing symptoms the best treatment is fulguration under local analgesia; in about 3 weeks healing takes place under the crust, which should be left undisturbed. Occasionally treatment may have to be repeated several times. Relapses should be dealt with in the same way. This method of treatment is stated to be particularly successful in children and young adults. Surgical treatment is indicated only where warts are very large or have not responded to treatment, and where previous treatment has resulted in scarring and ulceration. When a very large area is involved it may be necessary to cover the defect with a split skin graft or with a rotated flap from the heel. After surgical excision, however, it is estimated that complete freedom from disability can be expected in only 50% of cases. *X*-ray treatment is ineffective and dangerous and should never be used. The author bases his treatment on the assumption that the spontaneous disappearance of warts which sometimes occurs is due to immuno-biological reactions towards the virus causing them, and that these reactions can perhaps be stimulated by partial destruction of the wart or by the mild secondary infection following trauma. *A. Fessler*

734. **Treatment of Pemphigus with Potassium *para*-Aminobenzoate**

C. J. D. ZARAFONETIS, A. C. CURTIS, and J. M. SHAW. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **231**, 30–50, Jan., 1956. 8 figs., 21 refs.

Over a period of 6 years beginning in 1949 before the introduction of cortisone and ACTH 18 patients with various forms of pemphigus were treated at the University of Michigan and Temple University Hospitals with potassium *para*-aminobenzoate. The drug was administered in a 10% aqueous solution, usually 30 ml. (3·0 g.) every 3 hours for 6 to 8 doses daily—that is, a total of 18 to 24 g. a day. In 7 out of 10 cases of pemphigus vulgaris the clinical response was regarded as excellent; however, in 2 of the cases cortisone was also given. Marked improvement was obtained in 2 out of 4 cases of pemphigus foliaceus, but in 3 cases of pemphigus erythematosus the response was variable. Definite benefit was observed in one case of ocular pemphigus. The authors state that the only potentially serious complication of the treatment is hypoglycaemia; this can be avoided by interrupting treatment if the patient fails to eat for any reason at all. They conclude that potassium *para*-aminobenzoate alone or in combination with steroid hormones is valuable in the management of pemphigus. The paper contains a number of illustrations and detailed case histories. *E. W. Prosser Thomas*

735. **Treatment of Lupus Erythematosus with Mepacrine**

J. V. CHRISTIANSEN and J. P. NIELSEN. *British Journal of Dermatology* [*Brit. J. Derm.*] **68**, 73–87, March, 1956. 5 figs., 23 refs.

The authors describe, from the Finsen Institute, Copenhagen, the results achieved with mepacrine in the treatment of 97 cases of chronic lupus erythematosus all of the discoid or purely erythematous type. The drug was given initially in doses of 200 mg. daily, rising to 300 mg. until yellow pigmentation became marked (usually in about 21 days), and then reduced to 100 to 200 mg. daily; the mean total dose for the series was 18 g. given roughly at the rate of 1 g. per week. The period of follow-up ranged from 3 to 21 months (mean 9·7 months). The ratio of female to male patients was about 3 to 1. Little difference was observed between the results in the 56 patients treated in hospital and those (41) treated as out-patients.

There was an excellent result in one-third of the patients, and considerable improvement in a further third, the results being notably better in patients over 60 years of age. In both groups, however, there was a relapse rate of about 80% within a few months of stopping treatment. Side-effects occurred in 29 cases in the form of dyspepsia, dermatitis, and disorders of sweating, and necessitated suspension of treatment in 12 cases. The authors discuss their methods of evaluating improvement and subject their results to statistical analysis. (Since July, 1954, they have replaced mepacrine by chloroquine, and a report of the results with the latter drug is promised later.) *John T. Ingram*

736. **Silicone Barrier Cream in Prevention of Bedsores**
F. J. A. BATEMAN. *British Medical Journal* [*Brit. med. J.*] 1, 554–555, March 10, 1956.

The author noticed that some elderly patients who had been bedridden for a long time at home entered St. Mary's Hospital, Colchester (a geriatric hospital), with pressure areas in fairly good condition, but developed bedsores in so short a time as 2 or 3 days after admission, in spite of the usual routine care consisting in change of position, washing with soap and water, rubbing with spirit, and dusting with powder 5 times daily.

A new method of treatment was therefore instituted in which the changing of position was continued as before but the frequent washing and all rubbing with spirit was discontinued, pressure areas being washed only twice weekly unless soiled with excreta, and then with warm water only, and carefully dried. A barrier cream, silicone vasogen (" lactagol "), which consists of 20% polydimethylsiloxane in a water-soluble base, was smeared thinly over the pressure areas twice daily. In addition all patients received 25 mg. of tolazoline to improve the blood supply to the skin and 50 mg. of ascorbic acid, both 3 times daily. Since this regimen was introduced the incidence of fresh bedsores has been lower than before. In addition there has been a considerable saving of the nurses' time—a particularly important point in a hospital for chronic cases where staffing difficulties are acute. The cost of treatment is low, and there have been no cases of skin sensitization or conjunctivitis among patients or staff arising from use of the barrier cream. *E. H. Johnson*

737. **Studies of Besnier's Prurigo (Atopic Dermatitis).** [In English]
S. HELLERSTRÖM and H. LIDMAN. *Acta dermato-venereologica* [*Acta derm.-venereol. (Stockh.)*] 36, 11–22, 1956. 2 figs., 4 refs.

The authors state that Besnier's prurigo is now recognized as an allergic skin disease, usually affecting the face, neck, and flexures, with a constitutional background, and is distinct from other forms of eczema. They then present results of a study at Karolinska Sjukhuset, Stockholm, of 311 patients with this condition, noting that it is common in Sweden and accounts for one-sixth to one-fifth of all cases of skin disease. Furthermore, they believe that there has recently been an increase in its incidence. Its distribution is about equal between the sexes (52% females), and in 86% it appears during the first 5 years of life. The familial incidence of asthma is about 30%, of allergic rhinitis about 10%, and of Besnier's prurigo about 40%. [A definition of familial incidence is not given.]

The course of Besnier's prurigo is described [but the evidence is not readily assessable]. The eosinophil count was found to fall during treatment in hospital. In every patient the reactions to skin tests were investigated; positive reactions to food allergens were thought to be a valuable finding in children. Of the entire series, only 22 patients showed no response to intradermal or patch tests; the allergens provoking reactions are considered. The relationship between positive skin reactions and a family history of allergic conditions is discussed.

[The importance of allergy in Besnier's prurigo is not accepted by some authorities.] *S. T. Anning*

738. **The Influence of Isoniazid on the Development of Lupus Carcinoma.** (Einfluss von Isonicotinhydrazid auf die Lupuskarzinomentstehung)
K. POMPE. *Dermatologische Wochenschrift* [*Derm. Wschr.*] 133, 105–108, 1956. 7 refs.

The incidence of lupus carcinoma at the Dermatological Clinic of the University of Brno, Czechoslovakia, was 0·08% (1 case in 1,270 patients) before the advent of isoniazid. Since 1952, 150 patients with lupus vulgaris have been treated with isoniazid and of these, 7 (4·6%) developed carcinoma. It is assumed that the use of isoniazid is in some way directly concerned with the increase in the incidence of carcinoma.

[Incidences of lupus carcinoma as high as and higher than that found in this series treated by isoniazid have been reported elsewhere after treatment with other drugs.] *G. W. Csonka*

739. **Tetracycline Hydrochloride in the Treatment of Acne Vulgaris**
G. A. CRONK, D. E. NAUMANN, E. J. HEITZMAN, F. N. MARTY, K. J. MCDERMOTT, and A. A. VERCILLO. *A.M.A. Archives of Dermatology* [*A.M.A. Arch. Derm.*] 73, 228–235, March, 1956. 6 figs., 13 refs.

At the University of Syracuse, New York, tetracycline hydrochloride in a dose of 250 mg. four times daily was given to 72 students suffering from acne vulgaris; during the course of treatment no topical applications were used. After all the pustules had disappeared the dose was reduced to 250 mg. once or twice daily. On the average the result was a 50% reduction in the number of lesions at 30 days and a 62% reduction at 60 days; in 7 cases there was no response to the treatment. No correlation between the sensitivity of the associated bacteria to the antibiotic *in vitro* and the clinical response could be established. Diarrhoea was a complication in 7 patients, in 2 of whom treatment had to be discontinued, but in the others, even when treatment lasted as long as 272 days, there were no other adverse side-effects. All the patients who developed diarrhoea did so within the first 40 days of treatment. It is suggested that tetracycline may have some pharmacological action apart from its effect on bacteria. *E. Lipman Cohen*

740. **The Effect of Prolonged Tetracycline Therapy on the Sensitivity of Bacterial Isolates from Acne Patients**
C. A. CRONK, D. E. NAUMANN, and C. GARRISON. *Antibiotic Medicine* [*Antibiot. Med.*] **2**, 153–157, March, 1956. 1 fig.

A series of 51 patients suffering from acne vulgaris was studied at Syracuse University Health Service, New York. *Staphylococcus aureus* was isolated from the lesions in all cases before treatment and 33 of these cultures were resistant *in vitro* to tetracycline in concentrations of 4 μg. per ml. or more. The patients were then given tetracycline hydrochloride, 0·5 to 1 g. daily, for 18 to 210 days, with a reduction by 75% or more in the number of acne lesions in 99% of those whose staphylococci had been tetracycline-sensitive *in vitro* and in 90% of those with tetracycline-insensitive organisms. This difference is not significant statistically. Paradoxically, it thus appears that the sensitivity of the organisms to the antibiotic *in vitro* made little or no difference to the results of treatment with it. In 35 cases cultures were made at varying intervals during treatment. Of the organisms isolated, 62% showed no change in sensitivity to tetracycline, 22% showed increased resistance, and 16% showed decreased resistance.

E. Lipman Cohen

741. **Animal Reservoir of Ringworm Infection in Britain**
MEDICAL RESEARCH COUNCIL, MEDICAL MYCOLOGY COMMITTEE. *British Medical Journal* [*Brit. med. J.*] 1, 963–965, April 28, 1956. 7 refs.

A high proportion of human dermatomycoses in Britain are due to animal-type ringworm fungi, infections of this type predominating in the rural areas, although they are also common in urban districts. As a result of the activity of the public health and school authorities human dermatophyte infection is gradually being eliminated, but the animal reservoir of infection largely remains.

The infection of cats with *Microsporum canis* offers particular problems as its diagnosis usually requires examination under ultraviolet light for fluorescence, and several human contact cases may occur before a particular cat is suspect. When dogs are infected with this organism there are usually depilated areas which facilitate diagnosis. Cattle ringworm, which is most commonly due to *Trichophyton verrucosum* and may affect up to 15% of a herd, can be transferred to man, and provides its own problems.

In Leeds an experiment in the control of *M. canis* infection has been in progress in recent years, the school medical service, the public health service, and the hospital service having cooperated in the microscopical confirmation of suspected human cases and the examination and treatment of the cat and dog contacts as required. Apart from this the only diagnostic service available to general practitioners and pathologists has been provided by the Mycological Reference Laboratory of the Public Health Service at the London School of Tropical Medicine, while a similar service for animal mycoses has recently been provided by the Ministry of Agriculture, but arrangements have now been made to provide facilities for mycological diagnosis at the regional laboratories of the Public Health Service throughout England and Wales and at the 19 Veterinary Investigation Centres of the Ministry of Agriculture. It is hoped that, as a result of more accurate diagnosis, much valuable data concerning animal ringworm in man will be accumulated.

R. R. Willcox

742. **The Use of Mustard in the Treatment of Epidermophytosis.** (О применении горчицы в комплексе лечения больных эпидермофитией)
V. A. IGOSHIN. *Вестник Венерологии и Дерматологии* [*Vestn. Vener. Derm.*] **30**, 17–18, No. 2, March–April, 1956.

The use of mustard in the treatment of epidermophytosis is based on the claims that it possesses fungistatic and fungicidal properties, and that in the form of a mustard bath it inhibits hyperhydrosis. An aqueous solution of mustard has been shown to destroy *Trichophyton mentagrophytes* and *T. rubrum* in a dilution of 1 in 800 and *T. gypseum* in a dilution of 1 in 200. [This last species is generally regarded as identical with *T. mentagrophytes*.] This effect is attributed to allyl*iso*thiocyanate, a product of the action on a glycoside of the enzyme myrosin which occurs when the mustard comes in contact with water.

In the acute exudative stage of epidermophytosis dressings of an 0·5% aqueous solution of mustard are applied every 3 to 4 hours for 24 to 48 hours, after which foot baths in 1% mustard solution at 38° C. are given for 15 minutes morning and evening until desquamation is complete, that is, for 5 to 6 days. The patient then continues indefinitely to have mustard foot baths every evening, painting the affected areas with 2 to 3% iodine solution each morning. Hyperkeratotic forms are treated with mustard baths combined with the application of an ointment containing resorcinol and salicylic acid, while for mild, atypical cases mustard baths and painting with iodine solution are usually sufficient. It is emphasized that if secondary infection is present it should be eliminated before the treatment of the fungus infection is started.

In all, 390 patients have been treated by this method, 79 with the acute exudative type, 84 with the hyperkeratotic type, and 227 with mild atypical types of infection. In each group the average time of treatment was considerably shorter than in a comparable control group, the respective figures being 17·3 and 27·9 days for acute exudative cases and 12·3 and 18·9 days for hyperkeratotic cases. [The number of controls is not stated.] During a follow-up period of 6 to 12 months only 2 early relapses were reported. No complication due to the treatment was observed.

It is emphasized that for therapeutic use the mustard powder must be fresh and must not have been in contact with water previously.

H. Makowska

743. **The Microanatomy of Miliaria Crystallina**
G. W. HAMBRICK and H. BLANK. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **26**, 327–336, April, 1956. 5 figs., 9 refs.

Paediatrics

PREMATURITY AND NEONATAL DISORDERS

744. **Effect of Vitamin-K Dosage on Plasma-bilirubin Levels in Premature Infants**
J. P. BOUND and T. P. TELFER. *Lancet* [*Lancet*] **1**, 720–722, May 19, 1956. 1 fig., 7 refs.

The comparative effects of large and small doses of vitamin K (" synkavit ") on the plasma bilirubin level of premature infants on the fifth day of life were studied at University College Hospital, London. During the 8 months beginning September, 1954, 55 infants (Group A) each received an intramuscular injection of 10 mg. of synkavit daily for 3 days, while during the 7 months starting May, 1955, 51 infants (Group B) each received 1 mg. of synkavit intramuscularly on the first day of life. The mean bilirubin level on the fifth day of life in Group A was 15·4 mg. per 100 ml., and in Group B it was 9·7 mg. per 100 ml. The bilirubin level reached 18 mg. per 100 ml. or higher in 21 of the infants in Group A and in 2 of those in Group B. Two infants in Group A died from kernicterus, the plasma bilirubin levels on the fifth day in these 2 instances being 34 and 24 mg. per 100 ml. respectively. A further 3 patients in Group A in whom the bilirubin level was high had mild symptoms on the seventh day of life, but when the infants were seen at the age of one year, they appeared normal. None of the patients in Group B developed kernicterus.

This investigation shows that the dose of vitamin K given to premature infants affects the subsequent plasma bilirubin level and that a reduction in the incidence of kernicterus " can be anticipated if the practice of giving large doses of vitamin K analogues to premature infants is abandoned ". *R. M. Todd*

745. **Hematopoiesis in Premature Infants with Special Consideration of the Effect of Iron and of Animal-protein Factor**
J. A. WOLFF and A. M. GOODFELLOW. *Pediatrics* [*Pediatrics*] **16**, 753–762, Dec., 1955. 2 figs., 12 refs.

A study of the blood changes occurring in premature infants during the first 18 months of life was undertaken at the Babies Hospital and at Columbia University, New York. A total of 81 subjects was divided into two groups: (I) 45 weighing less than 1,200 g. and (II) 36 weighing 1,200 to 1,500 g. at birth. All the infants included in the study were admitted within 48 hours of birth, and none was accepted who had any disease, infection, or abnormality. The haemoglobin concentration, erythrocyte and reticulocyte counts, total and differential leucocyte counts, and platelet count were determined at birth, twice during the first week, and then once weekly during the rest of the first 12 weeks of life and the mean values for each group calculated. After discharge from hospital blood examinations were repeated, whenever possible, at monthly intervals for the rest of the infant's first year, but in many cases follow-up visits were sporadic or the baby developed an intercurrent infection and was therefore excluded from the later part of the study. The haemoglobin concentration was measured in a Klett photoelectric colorimeter, the platelets counted in a counting chamber by the direct method, and the reticulocytes counted after staining with brilliant cresyl blue. All the infants were fed a standard mixture of evaporated milk and sugar, with the addition of a multivitamin preparation daily after the 7th day. In each group 12 infants were given 16 mg. of iron daily, beginning within the first 10 days, 12 were given " animal-protein factor ", consisting of aureomycin, 5 mg., vitamin B_{12} (cyanocobalamin), 1·5 mg., and elemental iron, 0·3 mg., 3 times a day, starting within the first 3 weeks of life, and 12 were given no treatment, serving as controls. In addition, in Group I 9 infants were given supplements of 1 mg. of elemental iron daily after the first 10 days. At first a blood transfusion was given whenever the haemoglobin value fell below 7 g. per 100 ml. However, in one early case permission for transfusion was refused and although the value fell to 5·2 g. per 100 ml. despite iron therapy, the clinical course was uneventful. After this experience transfusion was never given for anaemia alone, but only in the presence of infection or poor clinical progress.

Neither the birth weight nor any form of treatment appeared to affect the fall in haemoglobin concentration which occurred during the first 12 weeks of life, the mean value falling in controls and treated patients in both groups alike to a minimum of 7 to 8 g. per 100 ml. at 8 to 9 weeks. The same was true of the fall in erythrocyte count, there being no statistically significant difference between the two groups. The reticulocyte count was high at birth, fell precipitously during the first 10 days to a mean value of 20% and then rose slowly to a second peak at the 8th week, when the haemoglobin value was at its lowest. The height of the first and second reticulocyte peaks varied inversely with the birth weight, but no treatment had any significant effect.

The mean platelet count in both groups rose from a mean of 150,000 per c.mm. at birth to 200,000 to 250,000 per c.mm. between the 6th and 12th weeks. Leucocyte counts showed great variation, but in general a polymorphonuclear neutrophil leucocytosis was present at birth, the count falling to below 12,000 per c.mm. and the proportion of lymphocytes rising from 33% to 60 or 70% by the 4th week. There was no consistent change in the monocyte count. The proportion of nucleated erythrocytes was over 15% in the first 8 days, falling to about 1% by the 4th day.

Despite the apparent lack of effect of treatment on the early phase of the anaemia of prematurity, it is claimed that in the untreated infants and those given animal-protein factor who were examined at the end of 12 months the haemoglobin values were well below the

normal range for full-term infants, whereas in those given iron the values came within the normal range. [The number examined at 12 months is not stated.]

A. White Franklin

746. **Blood Pigments in Haemolytic Disease of the Newborn**

D. C. A. BEVIS. *Journal of Obstetrics and Gynaecology of the British Empire* [*J. Obstet. Gynaec. Brit. Emp.*] 63, 68–75, Feb., 1956. 8 figs., 24 refs.

The author suggests that the concentrations of bilirubin and oxyhaemoglobin in the liquor amnii and the cord blood in cases of haemolytic disease of the newborn may provide a guide to the prognosis for the infant and an indication of the need for treatment to prevent the onset of kernicterus. To investigate this hypothesis and to study the natural history of the disease the pigments present in 71 specimens of liquor amnii obtained by abdominal paracentesis from 40 sensitized Rh-negative mothers, in 44 specimens of cord blood from cases of haemolytic disease, in 20 specimens of brain tissue, 4 of cerebrospinal fluid, and one tooth from cases of kernicterus, and in 4 specimens of yellow vernix caseosa from jaundiced infants were examined at Park Hospital, Davyhulme, Manchester. In all specimens indirect-reacting bilirubin was found, with the exception of the tooth, which contained biliverdin. Oxyhaemoglobin was usually also present.

The presence of a high concentration of both pigments in the liquor amnii was always associated with the subsequent development of kernicterus, and that of a high concentration of bilirubin alone with the development of haemolytic anaemia. The upper limit of normal concentration in liquor amnii of bilirubin is 0·42 mg. and of oxyhaemoglobin 1·67 mg. per 100 ml. The concentration of these pigments in the normal liquor amnii slowly increases from the 20th week, but the author states that haemolytic disease may develop rapidly at any time so that it is advisable for assessment of the condition of the foetus by this method to be carried out at intervals of not more than 2 weeks after the 32nd week.

The role of bilirubin in the production of kernicterus is discussed and the techniques used are described.

John Murray

747. **Incidence of Hemolytic Disease of the Newborn Due to A or B Incompatibility**

C. M. TURMAN, V. C. VAUGHAN, and R. M. SHELLY. *American Journal of Obstetrics and Gynecology* [*Amer. J. Obstet. Gynec.*] **71**, 885–890, April, 1956. 6 refs.

The importance of A and B incompatibility as a potential cause of kernicterus may be judged from the fact that of 13 children referred to St. Christopher's Hospital for Children, Philadelphia, over a period of 18 months with clinical evidence of cerebral damage due to kernicterus, the cause was unsuspected Rh incompatibility in 7 instances and A or B incompatibility in 5—in the remaining case there was hereditary spherocytosis, which may have been the cause. To ensure the early detection of icterus in the newborn a " jaundice round " is carried out by the nursing staff at 8-hour intervals in the newborn nurseries of the Abington Memorial and Temple University Hospitals, Philadelphia. If an infant less than 36 hours old is noted to be jaundiced the case is immediately notified to a responsible medical officer and steps taken to establish the probable aetiology of the jaundice. Investigations include the grouping and typing of the parents' and infant's blood, the performance of the Coombs test, and the " glue test " (examination of cells suspended in glue–saline for agglutination) on the infant's erythrocytes, and a search for immune anti-A or anti-B in the mother's serum. The haemoglobin content of the infant's blood is also determined. The results over a 6-month period showed the incidence of haemolytic disease due to A or B incompatibility to be 0·86%, the total number of deliveries being 2,672.

The acute phase of the disease is generally milder than that caused by Rh incompatibility, and is not responsible for stillbirth. Kernicterus probably occurs in 2 to 10% of clinically diagnosable but untreated cases. The treatment of A and B incompatibility consists in exchange transfusion to prevent the serum bilirubin level rising above 20 mg. per 100 ml. Fresh blood shown to be compatible with the mother's serum by the indirect Coombs technique is used.

John Murray

748. **Interstitial Emphysema, Pneumothorax, and " Air-block " in the Newborn**

J. L. EMERY. *Lancet* [*Lancet*] **1**, 405–409, April 14, 1956. 6 figs., 20 refs.

Interstitial emphysema of the lung and mediastinum and pneumothorax occur spontaneously in the newborn, without either infection or violent artificial respiration. Usually the infant is large, mature or postmature, has not required artificial respiration, and has cried lustily. Mucus is found round mouth and nose. In some cases there are no symptoms, the infant dying without warning, while in others death follows a cyanotic attack or a change in the character of respiration. The author discusses the clinical and pathological features of 14 cases seen during the last 5 years at the Children's Hospital, Sheffield, in which death within the first 7 days of life was due to spontaneous interstitial emphysema of the lungs and mediastinum, half of these cases being encountered at necropsy on 100 infants during the period 1954–5. Of this last group of 100 infants, 48 were premature, but none died from spontaneous interstitial emphysema; of the 52 full-time infants, 7 died from this condition, which, the author states, is the " commonest single cause of death in mature infants ".

Labour was normal in all except one of the 14 cases. There was asphyxia at birth in one; 11 died within the first 24 hours. The author suggests that symptomless interstitial emphysema occurs in one in 200 normal infants. Post-mortem examination revealed air vesicles in the interstitial tissue of the lung, which were larger as the hilum was approached. After fixation, air could be seen in the sheaths of vessels by the naked eye. There were no air emboli. The right heart was dilated, but the liver was not enlarged. Microscopically, masses of mucus, usually containing keratinized squames, were

seen in smaller bronchi and bronchioles, with dilated alveoli beyond and sometimes actual rupture. The immediate cause of death was air in the pleural cavity and mediastinum with compression of vessels at the root of the lungs producing " air-block ". The author states that the rupture is due to excessive expiratory effort after aspiration of mucus or meconium, and that pulmonary hypertension leads to cor pulmonale and death.

A. White Franklin

749. **Meconium Ileus. A Clinical Study of Twenty Surviving Patients**

H. SHWACHMAN, C. V. PRYLES, and R. E. GROSS. *A.M.A. Journal of Diseases of Children* [*A.M.A. J. Dis. Child.*] **91**, 223–244, March, 1956. 15 figs., 30 refs.

The authors, from the Children's Medical Center and the Harvard Medical School, Boston, review the historical aspects of meconium ileus, which is responsible for 15% of all types of neonatal intestinal obstruction. In 1938 Anderson established the association of meconium ileus with cystic fibrosis of the pancreas, and this was amply confirmed later by other workers, although absence of pancreatic enzymes is not the only factor leading to inspissation of the meconium. It appears that the production of an excessive amount of abnormal meconium by the gastro-intestinal glands in association with pancreatic achylia leads to meconium ileus.

The progress is reviewed of 20 patients who presented with meconium ileus in the neonatal period and who survived up to July, 1955, the eldest then being 8½ years and the youngest 5 months old. Treatment was surgical in 15 (Mikulicz resection with double-barrelled ileo-ileostomy, followed by closure of ileostomy 2 to 3 weeks later), and 5 were relieved by medical means (enemata, gastric lavage, and instillation of pancreatic enzymes). All developed cystic fibrosis of the pancreas. This was confirmed by laboratory studies, which showed absence of pancreatic enzymes from the duodenal juice and abnormally high sodium and chloride content of the sweat. Subsequent management consisted of a high-calorie (90 to 100 Cal. per lb. (0·454 kg.) body weight daily), low-fat diet with a protein intake of 1·5 g. per lb. body weight daily. Milk preparations with low curd tension are advised, together with multivitamin preparations in amounts twice the normal requirements and a liberal salt intake. Pancreatin is added on the introduction of solid food. In spite of early institution of antibiotic therapy, pulmonary symptoms and signs developed in the first few months of life in all but 3 patients. Radiographic changes consisted in irregular aeration, increased bronchovascular markings, lobular atelectasis, emphysema, and bronchiectasis. Lobectomy was performed with success in one case.

The main infecting agent was the staphylococcus. Attempts to remove obstructive plugs of mucus from the bronchi by the use of streptokinase and streptodornase or by aspiration through a bronchoscope were unsuccessful.

All the common antibiotics were used prophylactically, but once infection was established they were given in full therapeutic dosage, singly or in combination. A penicillin–streptomycin aerosol used for short periods was found effective. Most patients had continuous antibiotic cover from the time of admission.

Assessment of the children at the time of the report showed that 9 were at or above the 35th percentile in weight and 4 were below the 3rd percentile; 3 were free from pulmonary involvement; 6 had mild, 7 moderate, and 4 moderate to severe pulmonary involvement. [These grades are accurately defined.] The prolonged antibiotic treatment, which in 5 patients exceeded 5 years, did not produce serious toxic or deleterious effects, and moniliasis, avitaminosis, anaemia, or liver involvement did not arise. The family history showed that, out of a total of 41 pregnancies in the 20 families, 23 resulted in infants with meconium ileus, 2 in infants with cystic fibrosis, and 15 in normal infants.

It is considered that the belief that patients with meconium ileus represent the severest form of cystic fibrosis and have the poorest prognosis is no longer justified: the prognosis depends upon the severity and rate of progression of the pulmonary manifestations. Even these may regress in time. Of 61 patients operated on for meconium ileus between 1945 and 1955, 25 were relieved of their obstruction, but 8 of these died subsequently.

[This is an excellently presented report of valuable work and should be read in full by all interested in this problem.] *John Lorber*

CLINICAL PAEDIATRICS

750. **Pink Disease and Mercury in Sheffield, 1947–55**

T. COLVER. *British Medical Journal* [*Brit. med. J.*] **1**, 897–898, April 21, 1956. 11 refs.

Pink disease is relatively common in Sheffield and at the Children's Hospital a special clinic is devoted to the care of patients suffering from the disease. Sheffield was thus a suitable centre for the investigation of mercury as a possible aetiological factor in pink disease. In an earlier inquiry in the city in 1948 some 200 mothers of children aged 12 months to 2 years were asked whether they had given the children teething powders at the ages of 4 to 12 months. Of the 64 mothers who could remember doing so, 60 named the preparation; 52 of these preparations contained mercury. It was estimated that about one-quarter of the infants in Sheffield were receiving mercury in teething powders at the age when pink disease usually occurs.

In 1955 a similar inquiry among 200 mothers revealed that 39 had administered teething powders to their infants. Examination of 183 powders bought from local chemists and dealers showed that 131 did not contain mercury. As regards the prescribing of mercurials no exact information was available, but it was the impression of doctors and members of the Sheffield Pharmaceutical Committee that these were now rarely prescribed for infants. The author states that while no precise conclusion can be drawn, his findings do suggest that the proportion of infants in Sheffield receiving mercury powders today is nearer one-tenth than the previous estimate of one-quarter.

There was little change in the incidence of pink disease between 1947 and 1951 as revealed by the number of children resident within the city boundary who were referred to hospital, but in succeeding years there was a downward trend. Up to 1951 over 30 patients were seen each year; in the following 4 years the figures were 26, 21, 17, and 6 respectively. Thus if it could be shown that mercury ingestion had fallen during the same period there would be strong evidence of a connexion between mercury and pink disease. No direct data on this could be obtained, but the circumstantial evidence was suggestive—namely, that two firms ceased to include mercury in teething powders, a large amount of old stock was recalled from retailers, and the medical officer of health advised retailers of the dangers of mercury therapy to babies. These measures were initiated at about the same time that the downward trend in the incidence of the disease was observed. *J. G. Jamieson*

751. **Use of Zoxazolamine (Flexin) in Children with Cerebral Palsy. Preliminary Report**
E. H. Abrahamsen and H. W. Baird. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 749–751, March 3, 1956

At St Christopher's Hospital for Children (Temple University School of Medicine), Philadelphia, the authors have tried the effect of zoxazolamine ("flexin"), a new relaxant drug, on two groups of children. In 10 children with severe mental retardation and muscular spasticity a decrease in the muscle tone was achieved with doses ranging from 30 to 140 mg. per kg. body weight per day, side-effects occurring in 8, including vomiting in 3. Among 28 children with muscular spasticity associated with various psychomotor disorders improvement occurred with a dose of 50 mg. per kg. daily after 10 to 210 days. In 15 cases this was accompanied by increased motor ability, but in the remainder muscle tone was reduced without improvement of function. Side-effects occurred in 15 of the 28.
L. Michaelis

752. **Prophylactic Sulphadimidine in Children Subject to Recurrent Infections of Upper Respiratory Tract**
J. B. Burke. *British Medical Journal* [*Brit. med. J.*] 1, 538–541, March 10, 1956. 11 refs.

The results are reported of prophylactic sulphonamide therapy in 48 children awaiting tonsillectomy at the Hospital for Sick Children, Great Ormond Street, London. The investigation was carried out over a period of 8 months, including the winter, on the double-blind principle, half the children receiving 0·5 g. of sulphadimidine daily and half calcium lactate tablets of similar taste and appearance for 4 months, the treatment groups then being reversed for a similar period. It was found that 28 of the children fared better on sulphadimidine, 3 were worse, and 17 were unaffected. Tonsillar hypertrophy and cervical adenitis were favourably influenced, but nasal obstruction and the incidence of the common cold were not affected. In one child a skin rash developed, but otherwise there were no toxic reactions to the drug.

It is concluded that prophylactic sulphadimidine is worth a trial as an alternative to tonsillectomy in children subject to recurrent infections of the upper respiratory tract, and that if treatment is started early enough tonsillar hypertrophy and cervical adenitis may regress and tonsillectomy become unnecessary.
Kathleen M. Lawther

753. **The Surgical Treatment of Localized Pulmonary Emphysema in Infancy and Childhood.** (Traitement chirurgical de l'emphysème pulmonaire localisé du nourrisson et de l'enfant)
J. Mathey, J. P. Binet, and J. J. Galey. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **13**, 113–129, 1956. 6 figs., 12 refs.

Since 1948 the authors have performed operations for bullous emphysema on 12 children, 4 of them aged less than one year. Cases of bronchogenic cyst, bullae following staphylococcal pneumonia, and emphysema following bronchial obstruction are not included in this series, nor are cases with infection or associated pneumothorax.

The main symptoms were dyspnoea, cough, wheezing, and cyanosis; in 4 cases they were severe and acute, demanding immediate treatment. On examination there was difficulty in expiration, and in infants thoracic deformity. The radiograph showed a clear hemithorax with mediastinal displacement away from it. Usually the outline of the cyst could be seen, sometimes with septa. Especially in the lateral view the remaining healthy lung could usually be made out, but it was difficult to determine its extent. In other cases the cyst occupied only part of the hemithorax, and occasionally it contained fluid. The appearances tended to vary considerably from day to day and exact location was seldom possible. Bronchoscopy was not informative.

Although in some cases the condition may present acutely with serious danger to life, in others apparently similar in nature it may exist for several years with minimal symptoms. Spontaneous disappearance does not take place, and operation is indicated in all cases, the entire emphysematous area being excised without removal of normal lung tissue. Needle aspiration should never be attempted owing to the danger of pneumothorax, though decompression by simple drainage, usually with tracheotomy, may be life-saving as a preliminary to thoracotomy in cases of urgent dyspnoea. A careful exploration should always be made, when it will usually be found that only one lobe or part of a lobe is involved. In most of the authors' cases, unlike those in other reported series, the lesion lay in a lower lobe. In one case pneumonectomy was necessary, in 4 lobectomy, and in 7 segmental resection or local excision. The lesion sometimes consisted of a single cyst with a wall of fibrous tissue not lined by epithelium and might be loculated or septate, while in other cases the lung tissue was replaced by a system of air-containing cavities separated by fragile walls ("cotton-candy lung"). No evidence of a valvular connexion with a bronchus was found in the specimens excised, although in at least one case during the operation it was possible to inflate the

cyst by pressure on the anaesthetic bag, but not to deflate it by external pressure. No sign of bronchial obstruction was found, but the bronchi in the affected area appeared small, translucent, and of soft consistency, lending support to the suggestion of Shaw that the primary cause is a condition of bronchomalacia.

One patient, operated upon as an emergency, died. The others recovered without complications and with full expansion of the remaining lung. They have all been followed up, 6 of them for more than 3 years, and have remained well without recurrence.

M. Meredith Brown

754. **Shigellosis in the First Two Years of Life**
B. MRAVUNAC and D. WEBER. *British Medical Journal* [*Brit. med. J.*] **1**, 1080–1082, May 12, 1956. 2 figs.

In Yugoslavia about 5,000 cases of bacillary dysentery are notified annually—a figure which the authors consider to be "certainly far short of the actual total". In recent years the number of cases of shigellosis in children during the first 2 years of life has steadily risen, the maximum incidence occurring in the third quarter of the year. In this paper the authors analyse their experience of 221 such cases admitted to the Infectious Diseases Hospital, Zagreb, between June, 1949, and May, 1953, the youngest patient being a premature infant 6 weeks old.

At least 2 specimens of fresh faeces or 2 rectal swabs were taken in every case and plated on SS agar at the bedside. Proof of infection with *Shigella* was obtained in only 59% of the series, the clinical diagnosis being supported in the remainder by epidemiological evidence of close contact with a known case. Flexner strains accounted for almost two-thirds of the proven cases, the other strains represented being Sonne (29·2%), Shiga (4·6%), and Schmitz (2·3%).

In the majority of cases the disease took a mild form. The onset was sudden in 61% of cases, being fulminant in 6·25%. Pyrexia occurred in 50%, and diarrhoea was a constant finding. Relapse, which was more frequent in infants than in older children, occurred in 7·2% of cases. The mortality was 2·3%, 4 of the 5 children who died being less than one year old.

[No information is given about treatment; also in view of the reported increase in incidence of the disease, details of the drug sensitivity of the organisms isolated would have been of interest.] *I. M. Librach*

755. **Metabolic Significance of Nervous Symptoms due to Attacks of Vomiting with Ketosis in Children**
R. DEBRÉ, P. ROYER, and H. LESTRADET. *Journal of Pediatrics* [*J. Pediat.*] **48**, 409–437, April, 1956. 16 figs., 39 refs.

This paper records the results of comprehensive metabolic studies carried out at the Hôpital des Enfants Malades, Paris, on 14 children who presented with cyclic vomiting and ketonuria associated with severe nervous disorders. In 11 cases the nervous symptoms were shown to be due to hypokalaemic alkalosis, in 2 to acidosis and ketosis, and in the remaining case to a generalized loss of electrolytes with extracellular hypotonia. All the children in the first group had been treated with sodium bicarbonate, and the authors consider that this probably played an important part in the production of the electrolytic disorder. They point out that as the metabolic consequences of attacks of vomiting are varied in nature, management must be adjusted to meet the individual requirements in each case.

The clinical sign of most value in the diagnosis of electrolyte disturbances is the type of respiration, which is superficial in alkalosis, whereas hyperpnoea occurs in acidosis with ketosis. Nevertheless, biochemical investigations, electrocardiography, and even electroencephalography are necessary to establish the type and degree of the electrolyte and acid–base imbalance. Hypokalaemic alkalosis with ketosis quickly responds to the administration of potassium chloride in a dosage of 200 to 400 mg. per kg. body weight, but treatment should always be continued for 5 to 7 days. The treatment of acidosis with ketosis consists in the administration of 80 to 100 g. of water and 8 g. of sugar per kg. per day until all evidence of ketosis has disappeared.

J. M. Smellie

756. **Abdominal Migraine in Children**
H. G. FARQUHAR. *British Medical Journal* [*Brit. med. J.*] **1**, 1082–1085, May 12, 1956. 21 refs.

The relationship between migraine and the "periodic syndrome"—recurrent attacks of abdominal pain, vomiting, and headache—in children was studied in 112 cases seen at the Royal Liverpool Children's Hospital. In 54% one or both parents were subject to migraine, more often the mother, while 30% of the children themselves had headaches resembling those of classic migraine. Cases in which headache alone occurred, however, were excluded from the series.

The cases are divided into 6 groups according to the predominant symptomatology, and case histories characteristic of each group are given, but it is admitted that the groups merged into each other. (1) Attacks of vomiting alone occurred in 7 children with an average age of 2·75 years, the lowest in the series. [Some of these children would have been too young to mention pain in the abdomen or head, even if present.] (2) Recurrent headaches with vomiting occurred in 21 cases, in 10 of which the headache was migrainous. (3) Recurrent abdominal pain alone occurred in 9 children, on 2 of whom operations were performed without benefit. (4) In 24 children abdominal pain was accompanied by vomiting. (5) In 21 cases abdominal pain was associated with headache. (6) All three symptoms occurred in 30 children.

Although intelligence tests were not carried out, the children were frequently described as being above the average at school, and almost universally as being conscientious, tidy, and somewhat obsessive. Nervous tension frequently precipitated the attacks, and travel sickness appeared to be common, although the incidence was not determined. A barium-meal examination was carried out in 20 cases, the findings being normal in 13 and localized spasm of the alimentary tract, often in the duodenum, being noted in 7. Electroencephalography

showed abnormal slow activity in 12 out of the 20 cases in which it was carried out.

The author points out that the frequent family history of migraine, the migrainous type of headache in 30% of the children, and the precipitation of the attacks by "the very same factors that bring on an attack of migraine" suggest strongly that this syndrome represents a juvenile form of migraine. There is also some evidence of an association with epilepsy, and in 3 of the 112 children epileptiform symptoms accompanied the attacks. However, the dividing line between epilepsy and migraine is always difficult to define, and Moore's theory that the vasoconstriction at the onset of a migrainous attack may initiate an epileptic discharge through anoxia of the cortex is quoted. The prime importance of recognition of the condition by the surgeon is emphasized, the fact that it may give rise to abdominal pain alone being insufficiently appreciated. *Pamela Aylett*

757. **Chronic Ulcerative Colitis in Childhood**
J. HOLOWACH and D. L. THURSTON. *Journal of Pediatrics* [*J. Pediat.*] **48**, 279–291, March, 1956. 22 refs.

Between 1934 and 1953 a total of 18 children (6 boys and 12 girls) suffering from chronic ulcerative colitis were admitted to the Children's Hospital, St. Louis, Missouri. The age at onset varied from 18 months to 14½ years, and the duration of symptoms before admission from 5 weeks to 10 years. Of the 18 children, 13 were followed up, 8 of them for 8 to 21 years after the onset of the disease. In 4 the disease was inactive and in 2 it was chronically active; surgical treatment had modified the course of the disease in 4. The remaining 3 patients had died, death being due respectively to perforation of the colon, intestinal obstruction, and carcinoma of the colon. Complications of the disease included retarded growth and sexual development, carcinoma of the colon, arthritis, purpura, and recurrent oedema of the arms and legs.

It is concluded that chronic ulcerative colitis is more serious in children than in adults, and that carcinoma of the colon, often arising from multiple foci, occurs more often and at an earlier age than in unaffected children of the same age group. Surgical treatment, including colectomy, is essential in any acute toxic case and where there are severe complications; conservative treatment should be reserved for cases in which the symptoms are mild or moderate. *Kathleen M. Lawther*

758. **Nephritis in Childhood. A Clinical Assessment of the Ellis Classification**
N. S. CLARK. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **31**, 12–21, Feb., 1956. 7 refs.

An analysis of the clinical course of nephritis treated at the Royal Aberdeen Hospital for Sick Children between 1934 and 1952 showed that 239 cases conformed fairly closely to Ellis's Type 1, whereas only 8 could be described with certainty as of Type 2. In the remaining 24 cases the pattern of the illness differed in various ways from that described by Ellis, and the histories of these cases are reproduced in some detail. [It seems that in some cases haematuria was less noticeable than is usual in Type 1, and that in others nephrotic changes supervened, although this is not stressed in the case histories.] The author concludes that these cases are intermediate between Type 1 and Type 2, and that these are not different diseases, but "merely the two extremes of a single clinical picture which is capable of very considerable variation". *L. H. Worth*

759. **Value of Propantheline Bromide in Treatment of Enuresis**
D. LEYS. *British Medical Journal* [*Brit. med. J.*] **1**, 549–550, March 10, 1956. 1 ref.

Propantheline bromide ("probanthine") is an anticholinergic drug with a potency three times that of atropine. In the trial here described from Farnborough Hospital, Kent, it was used in the treatment of enuresis in 33 children [apparently of both sexes] between the ages of 5 and 15 years as follows: 15 mg. was given daily for 4 days, 30 mg. for the next 4 days, and then 45 mg. for the last 6 days; a control group of 32 comparable children received a placebo. The whole period of study lasted for 8 weeks, parents or guardians being asked to record the number of "wet" nights during the 2 weeks before treatment, the 2 weeks of treatment, and the 4 weeks after treatment. The author points out that about half the subjects in each group (15 and 14 respectively) were "deprived" children, that is, separated from their parents and living in a children's home.

Propantheline was found to have a small (5%) but statistically significant effect in reducing the frequency of bed-wetting during treatment, but the difference between the two groups largely disappeared on cessation of treatment. The author emphasizes the necessity for treating the total emotional situation in these children, and concludes that even the slight relief afforded by such a drug as propantheline in a condition so complex as enuresis can be of great value. *E. H. Johnson*

760. **A Controlled Trial of Propantheline in Bed-wetting**
R. M. MAYON-WHITE. *British Medical Journal* [*Brit. med. J.*] **1**, 550–552, March 10, 1956. 4 refs.

Propantheline ("probanthine") partially blocks the parasympathetic innervation to the bladder and thus has a powerful depressant action on the detrusor muscle; it also causes fewer side-effects than most anticholinergic agents. The author describes a small-scale trial of its use in the treatment of enuresis in 9 young male patients (average age 6·2 years) attending the Ipswich and East Suffolk Hospital enuresis clinic; a group of 6 boys (average age 9·4 years) served as controls.

The study was divided into 3 periods of 4 weeks each; in the first the child was given one tablet (15 mg.) of propantheline at bed-time, in the second period 2 tablets, and in the third 2 similar but inert tablets. In the control group this regimen was reversed, the placebo being given during the first 2 periods and propantheline in the third. Finally there was a follow-up period without tablets during which the number of "dry" nights was recorded. In both groups there was a tendency to

improvement during the time of treatment, which persisted into the follow-up period, but since the extent of improvement was the same in both groups, the author concludes that propantheline is without effect in the treatment of bed-wetting. *E. H. Johnson*

761. **Flea Infestation as a Cause of Papular Urticaria. A Preliminary Investigation**
R. M. Bolam and E. T. Burtt. *British Medical Journal* [*Brit. med. J.*] **1**, 1130–1133, May 19, 1956. 6 figs., 16 refs.

The intensely irritating papular urticaria seen in young children is generally referred to by the mothers as " heat spots ", and claimed by them to be due to dietary indiscretions, usually an over-indulgence in fruit. The eruption, which often shows lesions of varied type at the same time, does not resemble allergic urticaria in the adult. The authors of the present paper attempted to show that the condition is a parasitic infestation, and for this purpose visited the homes of the affected children where a search was made for parasites. In 21 out of 30 cases fleas were found or were hatched out from dust samples which were collected, examined, and incubated under standard conditions of humidity and temperature. Five different species of flea were found, the cat-flea being the commonest; there was only one case in which infestation was due to the flea parasitic on human beings. Pets were kept in 20 of the houses visited; other possible sources of infestation were birds' nests and pets kept by neighbours. Measures for disinfesting homes and pets resulted in a clearance of the eruption in most cases. *Marianna Clark*

762. **Thrush Napkin Rashes**
J. P. Bound. *British Medical Journal* [*Brit. med. J.*] **1**, 782–784, April 7, 1956. 2 figs., 5 refs.

Thrush infection of the napkin area is not as rare as has been thought hitherto. Of 1,300 babies born at University College Hospital, London, over a 12-month period, 3% were known to have been affected by the age of 6 months. The rash is distinctive and a clinical diagnosis can usually be made with accuracy. Of 47 cases thus diagnosed, yeasts were subsequently isolated from swabs of skin in 42; no yeasts were cultured from specimens from 28 infants with other types of napkin rash or from 15 healthy controls. Yeasts could be isolated from the intact perianal skin of about one-half of the infants with oral thrush, but only 12 of the 42 children with proved thrush infection of the napkin area had concomitant oral thrush.

The sites most commonly affected were the buttocks and the inner side of the thighs. The early lesions were small, dull-red patches, which later coalesced. Desquamation occurred after the formation of small, flat, superficial vesicles. The only common rash with which this condition can be confused is seborrhoeic dermatitis in the napkin area, although in the latter condition there is no white, desquamating epithelium. Treatment was by application of a 0·1% aqueous solution of merthiolate after each change of napkin, followed by titanium dioxide paste, the latter acting as a protective covering in all types of napkin rash. There was a significantly increased incidence of thrush vaginitis in the mothers of affected infants, and the author suggests that the hands of the mother become contaminated, infection being transferred to the infant's skin when the napkin is changed. Previous treatment with antibiotics appeared to play little part in the aetiology of the condition. *Marianna Clark*

763. **The Treatment of Infantile Eczema.** (Traitement de l'eczéma du nourrisson)
R. Debré, P. Mozziconacci, N. Masse, and Y. Dupuy-Joie. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **13**, 1–15, 1956. 30 refs.

The authors describe their experience at the Clinique Médicale des Enfants, Paris, in the treatment of 43 cases of infantile eczema with cortisone. In view of the need for close supervision during cortisone therapy, only infants with severe generalized eczema or with excessive pruritus or repeated infections were so treated, and then only after other recognized forms of treatment had been tried and proved inadequate. Cortisone was not used in the presence of any evidence of oedema. The authors stress the necessity for continuing treatment with small and infrequent doses after the acute attack has subsided to prevent the otherwise inevitable recrudescences, the aim being not to produce a complete cure but to maintain the skin in a relatively satisfactory condition until the infant reaches the age of 18 months or 2 years, when it is to be presumed that the eczema will disappear spontaneously. Cortisone was given at first intramuscularly and subsequently by mouth, 100 mg. being given daily in 3 doses for 2 days, 75 mg. for 2 days, and then 50 mg. for 2 days. Thereafter in most cases 50 mg. was given at intervals increasing progressively up to one week and eventually, if possible, to 2 weeks. A salt-free diet was given throughout, and an antibiotic (usually oxytetracycline) concomitantly with the cortisone.

Among the earlier cases in the series, which received more prolonged treatment with a high dosage, hypertension developed in 3 and pulmonary oedema in 2, but among 31 infants given the above dosage there were no such troubles. Four infants died—one from pneumococcal meningitis, one from hyperpyrexia due to hypersensitivity to penicillin, and the other 2 from a severe staphylococcal infection. After the initial stages of treatment 18 of the 43 infants were cured, in 12 the condition was " improved ", and in 13 it was " slightly improved ". Of the 30 who subsequently continued to receive intermittent cortisone therapy, 17 were " much improved " and 14 " improved ", while in 2 cases the condition remained stationary. Local lesions responded well to treatment with hydrocortisone ointment, but relapsed immediately if it was omitted.

An attempt was also made to evaluate the use of aspirin given together with small doses of cortisone in the subacute phase, and also after the withdrawal of cortisone. The results were very satisfactory in 5 of the 8 infants treated, but the dose required to produce these results was very near the toxic level and the infants required careful watching. *Wilfrid Gaisford*

Public Health and Industrial Medicine

764. **An Endemiological Study of Enteric Virus Infections. Poliomyelitis, Coxsackie, and Orphan (ECHO) Viruses Isolated from Normal Children in Two Socio–Economic Groups**
E. I. Honig, J. L. Melnick, P. Isacson, R. Parr, I. L. Myers, and M. Walton. *Journal of Experimental Medicine* [*J. exp. Med.*] **103**, 247–262, Feb. 1, 1956. 4 figs., 13 refs.

An endemiological investigation of enteric virus infections was carried out over a 2½-year period among 136 healthy children from two socio-economic groups in Charleston, West Virginia. A total of 1,558 specimens of stool were examined and 77 viruses were isolated in tissue culture, 15 being identified as poliomyelitis viruses (14 Type 1 and one Type 2), 29 as Coxsackie, and 33 as enteric cytopathogenic human orphan (ECHO) viruses. Of the specimens from the higher socio-economic group 3% were positive on culture, whereas in the poorer group 8% of specimens were positive. Over 90% of the positive cultures were obtained during the months June to October. In nearly half of the children and contacts from whom poliomyelitis virus was isolated there was an associated increase in minor illnesses; no unusual incidence of such illnesses was noted in the group harbouring ECHO virus. In several in the former group there was a transient increase in neutralizing antibody titre against types other than the infecting type of poliomyelitis virus, in addition to a more persistent rise in antibody titre against the infecting strain.

D. G. ff. Edward

765. **Investigation of Diphtheria Infections in Kiev during 1952.** (Изучение заболеваемости дифтерией в 1952 г. в Киеве)
T. G. Filosofova, A. B. Shekhter, and A. K. Zavoĭskaya. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Zh. Mikrobiol.*] 64–69, No. 4, April, 1956. 9 refs.

Since 1950 the average proportion of immunized children in Kiev giving a positive Schick reaction has been comparatively high, being approximately 25%. Out of 307 children admitted to hospital during 1952 with diphtheria, 155 (50·4%) had been fully immunized with 3 or more injections of prophylactic, 61 (20%) had been incompletely immunized (less than 3 injections), and 65 (21·2%) had not been immunized. (The immunization records of 26 (8·4%) of the children could not be traced.) Generally, the clinical course of the diphtheria was mild, 86% of the cases consisting of faucial infections. Complications arose in only 12 cases, but 5 ended fatally.

In view of the inadequate level of immunity in the child population disclosed by these figures it is suggested (1) that the immunization campaign should be intensified, aiming at reducing the proportion of partially immunized or unimmunized children, and (2) that a prophylactic of higher antigenicity should be produced.

[This paper demonstrates that the difficulties recognized in Great Britain more than 10 years ago and overcome since then have not as yet been dealt with effectively in the U.S.S.R., although in the Ukraine a diphtheria immunization campaign on a large scale has been carried through since 1933.] *K. Zinnemann*

766. **Acute Upper Respiratory Infections in Families**
C. Buck. *American Journal of Hygiene* [*Amer. J. Hyg.*] **63**, 1–12, Jan., 1956. 1 fig., 17 refs.

Accepting the premise that infections occurring in successive members of a family within a short period of time are more likely to be related to each other than to be separately acquired from outside sources, the author attempted to verify some of the reported observations on the epidemiology of the common respiratory diseases. At monthly intervals 45 families (164 persons) in London, Ontario, received a form for recording the occurrence of colds in all members of the family, particularly the date of onset, symptoms, and approximate date of recovery. Of these 45 families, 35 reported for two 6-month periods, from November, 1952, to May, 1953, and November, 1953, to May, 1954; the other 10 families reported for the first 6-month period only, after which they left the district.

The analysis showed that there were 3·6 attacks of the common cold per person per year. Pre-school and school children introduced colds into the family much more frequently than did infants or adults, and the adult female, other than the housewife, more frequently than the adult male. The age of the subject with an index cold—that is, a new cold beginning 5 or more days after the onset of the last cold in the family—had more influence on the secondary attack rate (S.A.R.) than did the age of the exposed subject; for example, the highest S.A.R. from an index cold in the age group 2 to 4 years was observed among exposed infants under 2 years, and the highest S.A.R. from an index cold in the age group 5 to 14 was found among those exposed in the age group 2 to 4 years. The S.A.R. was higher in crowded conditions only when the index case occurred in children under 15. The incubation period of non-coryzal illness with sore throat (6·8 days) was longer than that of all other upper respiratory tract infections (4·7 days). Among children under 15 years the " symptom type " of secondary cold was significantly related to that of the index cold, but this did not hold good for adults. There was no evidence of immunity after an attack in children under 2 years, but rather of increased susceptibility for about 2 months; conversely, among pre-school children and adults there was some short-term immunity after an attack. Smoking did not appear to influence susceptibility to infection. *Kenneth Marsh*

INDUSTRIAL MEDICINE

767. **Factors Influencing the Radiological Attack Rate of Progressive Massive Fibrosis**
A. L. COCHRANE and W. E. MIALL. *British Medical Journal* [*Brit. med. J.*] **1**, 1193–1199, May 26, 1956. 3 figs., 24 refs.

This paper from the Pneumoconiosis Research Unit of the M.R.C., Llandough Hospital, Cardiff, describes an experiment designed to test the hypothesis that progressive massive fibrosis (P.M.F.) is caused by the infection with tuberculosis of patients suffering from simple pneumoconiosis, the tuberculous process being modified by the dust.

From the examination of radiographs taken in 1947 and again in 1949 the rate of appearance of P.M.F. among coal-miners living in Valley A, where a campaign was recently conducted to diagnose tuberculosis at the earliest possible stage and to isolate all known sources of infection, was compared with that among miners living in Valley B, where there had been no such campaign. In addition, Mantoux tests were carried out on the children in both areas in 1950–1 and again in 1954.

In Valley A there was a statistically significant reduction in the incidence of Mantoux positivity during the period between the tests, whereas in Valley B the reduction, though present, was not significant. The rate of appearance of P.M.F. was also lower in Valley A, the rate being 2% per year (11 cases) in 2,126 miners compared with 3·2% per year (19 cases) in 2,251 miners in Valley B. Statistical analysis shows that this difference could have occurred by chance in only 17% of such experiments.

The results of this investigation therefore tend to support the hypothesis that P.M.F. results from tuberculous infection, but they are in no way conclusive.

Kenneth M. A. Perry

768. **Fibrogenic Activity of Different Forms of Free Silica. The Action of Fused Silica, Quartz, Cristobalite, and Tridymite on the Livers of Mice**
S. H. ZAIDI, E. J. KING, C. V. HARRISON, and G. NAGELSCHMIDT. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **13**, 112–121, Feb., 1956. 13 figs., 9 refs.

This is the report of an investigation at the Postgraduate Medical School of London and the Safety in Mines Research Establishment, Sheffield, into the difference in pathogenicity of different forms of free silica—fused silica, quartz, cristobalite, and tridymite—and the intensity of tissue reaction in the livers of mice; also to discover if the response was the same as that observed in the lungs of rats (*Brit. J. industr. Med.*, 1953, **10**, 9; *Abstracts of World Medicine*, 1953, **14**, 1).

Acellular collagenous silicotic nodules were produced most rapidly by tridymite, cristobalite being next and quartz third; fused silica was the least fibrogenic. The splenic reaction to the various dusts was very slight, particularly to tridymite, the only evidence of any tissue reaction consisting in the laying down of a few compact reticulin fibres; no silicotic nodules could be discerned in any of the spleens. The rate of production of fibrosis in the livers of the mice was no faster than in the rat lungs of the previous experiment, nor did the fibrosis progress to as completely collagenous and confluent a state.

The authors are unable to offer a satisfactory explanation of the differences in pathogenicity of the various forms of crystalline and fused silica, but suggest there must be factors other than silica solubility. The fact that these silica dusts are markedly different in pathogenicity despite their being of the same solubility is possibly related to the character of the surface of the particles, which in its turn should be related to their crystalline structure or lack of it. *Kenneth M. A. Perry*

769. **Fibrogenic Activity of Free Silica of Different Particle Sizes. Tissue Reactions in Lungs of Rats and Livers of Mice to Different Doses of Ground Flint of Constant Surface Area**
S. H. ZAIDI, E. J. KING, C. V. HARRISON, and G. NAGELSCHMIDT. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **13**, 122–132, Feb., 1956. 11 figs., 8 refs.

In experiments carried out to decide the most pathogenic size of silica particles, which, it is pointed out, is of importance in the study of silicosis, flint dusts of different particle sizes were injected intratracheally into rats and intravenously into mice. The results support the hypothesis that fibrogenesis is closely related to the silica surface, and also indicate a range of maximally fibrogenic sizes. The amounts of different size fractions were chosen to yield equal surface areas of the particles contained. The size of particles ranged from 0·5 to 4 μ in the experiments on rats and from 0·2 to 4 μ in those on mice. The size of silica particle which was found to produce the maximum amount of fibrosis in the lungs of rats had a diameter between 1 and 2 μ, particles smaller or larger than this being less fibrogenic. The intravenous injections in mice showed that the size of flint particles producing maximum liver fibrosis lay between 0·2 and 2 μ in diameter—a rather wider range than that found in the lungs of rats.

Kenneth M. A. Perry

770. **The Silica-solubility Theory of Silicosis. II. Present Difficulties of Interpretation**
E. J. KING, S. H. ZAIDI, and G. NAGELSCHMIDT. *A.M.A. Archives of Industrial Health* [*A.M.A. Arch. industr. Hlth*] **13**, 133–138, Feb., 1956. 1 fig., 22 refs.

It was for long thought that silicotic fibrosis was a response of the tissues to an abrasive action by the particles of powdered quartz and other forms of free silica, until Gardner in 1923 showed that the particles of carborundum, which are as hard, sharp, and abrasive as those of powdered quartz, did not appear to produce a similar amount of fibrosis. In 1932 Kettle showed that quartz particles previously coated with a thin layer of iron oxide, which did not alter their microscopical appearance or their sharpness, did not produce silicosis in animals, and suggested the solubility theory, which

postulates that the particles of quartz, flint, and other forms of free silica are fibrogenic and produce silicosis because they slowly and persistently release silicic acid from their surfaces. This theory was further supported by the work of Denny *et al.*, who showed that the coating of quartz particles with aluminium hydroxide lowered both their solubility and their pathogenicity.

The present authors, in subjecting the solubility theory to further critical study, refer to their own findings [see Abstracts 768 and 769] that different specimens of quartz, of identical composition but of markedly different solubility, may have the same fibrogenic effect on the lungs of animals; that different forms of free silica, of identical chemical composition, may have a very similar solubility yet, given in amounts which ensure similar surface areas, may have markedly different fibrosis-producing capacities in animals; and, lastly, that the same minerals prepared in different ways, with similar particle size distribution, surface areas, and composition, may have appreciably different solubilities and yet produce similar degrees of fibrosis, and at the same rate, in animals. These facts, they maintain, suggest that the solubility theory should now be abandoned, since there are serious difficulties in the way of interpreting many facts in connexion with silicosis on the basis of solubility. *Kenneth M. A. Perry*

771. **Prevalence of Coronary Heart-disease in Elderly Coal-workers**

A. J. THOMAS, J. E. COTES, and I. T. T. HIGGINS. *Lancet* [*Lancet*] **1**, 414–420, April 14, 1956. 3 figs., 39 refs.

Some earlier clinical studies on the part of one of the present authors pointed to a high incidence of heart disease among miners. For instance, an analysis of the findings at necropsy on 1,000 coal-workers revealed 244 cases of coronary heart disease; in two-thirds of the cases the disease had contributed to death. Of an independent series of 134 hospital patients in South Wales suffering from pneumoconiosis, 44 had shown marked evidence of coronary disease, 20 of these being in the age group 55 to 64 years. There were, however, obvious objections to drawing general conclusions from this material, and a further investigation was therefore carried out to determine whether the findings applied to all miners and ex-miners in the older age-groups living in the area.

From a population of 1,160 miners and ex-miners aged 55 to 64 in the Rhondda Fach Valley, 55 were selected at random for the investigation. For various reasons 8 were unsuitable, the other 47 being subjected to a searching examination. The criteria for diagnosis of coronary heart disease were characteristic chest pain, unexplained left ventricular enlargement, and electrocardiographic evidence of coronary insufficiency. Of the 47 miners, 18 had coronary heart disease. The mean age of these men (61·1 years) and the average number of years they had worked underground and at the coal face did not differ significantly from the averages for the remainder.

In about one-half of the cases symptoms were present; in the rest the disease was silent. The mean systolic and diastolic blood pressures in the group with coronary disease (165·8 and 89·4 mm. Hg) were higher ($P<0·05$) than those for the remaining men in the sample (139·5 and 80·7 mm. Hg). The average weight of the men with heart disease was also higher—156·9 lb. (71 kg.) compared with 133·8 lb. (60·8 kg.)—but in view of the wide variation and the small number of patients the significance of this finding is difficult to assess. No significant relationship was established between coronary disease and smoking, but here too the small numbers rendered the results uncertain.

The authors discuss their findings in relation to other published figures and emphasize the need for further investigations of this type. *R. E. Lane*

772. **Neurosis in Telephone Operators.** (La névrose des téléphonistes)

—. LE GUILLANT, —. ROELENS, —. BEGOIN, —. BÉQUART, —. HANSEN, and —. LEBRETON. *Presse médicale* [*Presse méd.*] **64**, 274–277, Feb. 15, 1956. 6 refs.

Attention is drawn to the increasing incidence of minor mental and nervous disturbances among telephone operators. These symptoms have been recognized for some time, but according to the authors have generally been either minimized or wrongly interpreted. The present paper reports the results of a study of female operators in the central telephone exchanges in Paris, in whom the authors describe a number of symptoms which, they claim, form the following recognizable syndrome.

(A) *Nervous Fatigue.* Practically no telephonist is free from this feeling, and one in every 3 suffers from profound apathy at the end of the day. A common complaint is that of feeling " empty headed ", and of continually making stupid mistakes. Intellectual activity becomes impossible, many operators barely managing to read a newspaper. (B) *Changes of Mood and Personality.* Many operators who were once calm and reserved have the impression that they have changed and are now irritable and aggressive. They reply tartly when spoken to, while almost any noise, but particularly a sudden one, may precipitate a nervous crisis. On the other hand 32% become depressed, and contemplate or even attempt suicide. (C) *Sleeping Difficulties.* Only 14% sleep normally; 34% are tired all day; 53% have restless nights with nightmares; and 38% report periods of almost complete insomnia lasting for months. (D) *Somatic Troubles.* At work telephonists complain of palpitations and of pains in the thorax and stomach. Headaches are common, being frequent and persistent in 34%. Many suffer from digestive troubles, with gastric pains and vomiting.

The symptoms begin to appear in mild form during the first year of work, being engendered by the pace of the work and by the strict supervision. The operators feel harassed, although they do not find the operation itself difficult. It is postulated that this syndrome represents a case of true " experimental neurosis " characterized by damage to the processes of internal inhibition. It is argued from this that the remedy lies in changing the conditions of work. *R. Conrad*

Forensic Medicine and Toxicology

773. **An Electroencephalographic Examination of the Effects of Megimide and Daptazole in Barbiturate Narcosis**

J. M. PEACOCK. *Electroencephalography and Clinical Neurophysiology* [*Electroenceph. clin. Neurophysiol.*] **8**, 289–298, May, 1956. 3 figs., 10 refs.

The author, working at the Alfred Hospital, Melbourne, has studied 26 electroencephalograms (EEGs) obtained from 12 individuals who were undergoing treatment with " megimide " (bemegride) and " daptazole " (amiphenazole), 10 having been admitted unconscious as a result of barbiturate poisoning, while the other 2 were healthy males who were given a known dose of barbiturate intravenously before treatment was started. This consisted in successive intravenous injections of 0·05 g. of bemegride and 0·015 g. of amiphenazole at brief intervals over periods of 40 to 90 minutes. There was no similarity between the records of individuals suffering from the effects of different barbiturates, and the changes induced in the EEG by treatment followed no specific pattern. It is therefore concluded that electroencephalography is of no help in assessing the efficacy of treatment or in predicting the onset of toxic symptoms resulting from overdosage of the barbiturates.

John N. Walton

774. **Peripheral Neuropathy Caused by Arsenical Intoxication: A Study of 41 Cases with Observations on the Effects of BAL (2 : 3 Dimercapto-propanol)**

A. HEYMAN, J. B. PFEIFFER, R. W. WILLETT, and H. M. TAYLOR. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 401–409, March 1, 1956. 3 figs., 16 refs.

The authors describe and discuss 41 cases of acute and chronic arsenical poisoning with peripheral neuropathy seen at Duke University Hospital and the Veterans Administration Hospital, Durham, North Carolina, during 15 years. The principal criterion in selecting these cases was the excretion in the urine of more than 0·1 mg. of arsenic per 24-hours; and confirmatory evidence of arsenical intoxication was obtained in 11 cases by analysis of hair or viscera at necropsy. The source of arsenic was not determined in 24 of the cases; in 4 ingestion was accidental; in 7 it was thought to be due to direct contact with arsenate sprays and dusts, and in 5 to consumption of contaminated bootleg whisky; in the one remaining case, in which the diagnosis was made only post mortem, administration had been homicidal.

The clinical features of the intoxication are described in detail. In most cases the onset was generally sudden, with acute nausea, vomiting, and diarrhoea. Less commonly there was a gradual onset with the development of sensory disturbance in the extremities. Cutaneous manifestations were noted in 21 of the cases, usually appearing one to 6 weeks after onset. These consisted mostly in diffuse, branny desquamation over the trunk and extremities, often accompanied by dark pigmentation of large portions of the skin, and hyperkeratotic scaling lesions on the palms and soles. Pitting oedema was sometimes present, usually confined to feet and legs. Respiratory infection occurred in 11 cases. Transverse white striae were noted in the finger-nails of 21 patients, a sign which, the authors state, takes 30 to 40 days to develop, but they do not regard these lines as pathognomonic of arsenical poisoning. General symptoms referable to the central nervous system were headache, poor memory, and drowsiness. Symptoms of peripheral neuropathy were usually noted one to 3 weeks after exposure to arsenic and took the form of paraesthesiae of the feet and later of the hands, followed by severe symmetrical muscular weakness of the extremities and subsequent muscular atrophy.

Detailed laboratory findings are presented. High levels of arsenic were found in either the urine or the hair in all 40 of the cases in which analyses were carried out. The differential diagnosis of arsenical neuropathy is discussed, and the authors suggest that the disease should be considered in all patients with symmetrical peripheral nerve lesions who live in areas where arsenical compounds are used as pesticides. Treatment was on general lines, with the addition in some cases of courses of BAL (dimercaprol), the usual dosage being 2·5 mg. per kg. body weight intramuscularly every 4 hours for the first 2 days and once or twice a day thereafter for 9 to 15 days. The authors found that dimercaprol administered 7 days or more after exposure to arsenic had little effect on the subsequent course of the neuropathy; despite this they maintain that such therapy is indicated in arsenical poisoning, particularly in early cases. Microscopical study of biopsy specimens of peripheral nerve showed destructive changes consisting in fragmentation and resorption of myelin and disintegration of axis cylinders in early cases, with atrophy and interstitial fibrosis as later findings. The central nervous system was normal in those cases examined post mortem.

P. N. Magee

775. **Nystagmus as a Physical Sign in Alcoholic Intoxication**

D. E. HOWELLS. *British Medical Journal* [*Brit. med. J.*] **1**, 1405–1406, June 16, 1956. 3 refs.

776. **Exclusion of Parentage by Rh-Hr Blood Tests. A Modification of Boyd's Compact Tabular Presentation**

A. S. WIENER and I. B. WEXLER. *Journal of Forensic Medicine* [*J. forensic Med.*] **3**, 67–71, April–June, 1956. 4 refs.

Anaesthetics

777. **Anaesthesia for Operative Obstetrics: Value of Cuffed Endotracheal Tube**
D. COLEMAN and B. L. DAY. *Lancet* [*Lancet*] **1**, 708–709, May 19, 1956. 15 refs.

In this article from St. George's Hospital, London, the authors seek to show that inhalation of gastric contents during or immediately after anaesthesia in labour can be prevented by the use of a cuffed endotracheal tube. They cite American workers who estimate that aspiration of vomit accounted for 1·5 to 2·5% of all maternal deaths in the U.S.A., and point out that for Britain the figures are believed to be higher. Besides maternal deaths, maternal morbidity and foetal mortality have to be taken into account [no figures are given for these].

The duration of labour, the patient's food requirements during that time, and the pain and fears, which cause delayed gastric emptying, make adequate preoperative preparation impossible. Gastric lavage and aspiration of stomach contents are not only often inadequate, but also increase distress. In those cases in which it is necessary to empty the stomach a large-bore oesophageal tube should be used. During induction of anaesthesia a tipping table is necessary for the treatment of active vomiting or regurgitation and efficient suction apparatus and a laryngoscope must be available. After premedication with 1/100 gr. (0·65 mg.) of atropine and insertion of a Gordh needle into a vein, anaesthesia is induced in the horizontal position with a mixture of cyclopropane, oxygen, and nitrous oxide given through a closed circuit with a leak and with the absorber cut out. When the patient is unconscious succinylcholine chloride is given in dosage of 5 mg. per 14 lb. (0·78 mg. per kg.), and after gentle inflation of the lungs with oxygen, which does not encourage regurgitation into the pharynx, a cuffed endotracheal tube is inserted. The cuff is inflated and artificial respiration is continued until spontaneous respiration returns. The anaesthesia is maintained with gallamine triethiodide, cyclopropane, nitrous oxide, and oxygen, with assisted respiration if necessary. At the end of the operation pharyngeal and tracheobronchial toilet is performed before the cuff is deflated and the tube removed.

The authors discuss the advantages of this technique in protecting the lungs from inhalation of vomit and in maintaining good oxygenation at all times. They concede that it is comparatively complicated, but stress that obstetric anaesthesia requires experienced anaesthetists.

Raymond Vale

778. **The Potentiating Action of Chlorpromazine**
M. S. SADOVE, R. C. BALAGOT, and R. M. REYES. *Current Researches in Anesthesia and Analgesia* [*Curr. Res. Anesth.*] **35**, 165–181, May–June, 1956. 13 figs., 13 refs.

779. **Postanesthetic Nausea, Vomiting, and Retching. Evaluation of the Antiemetic Drugs Dimenhydrinate (Dramamine), Chlorpromazine, and Pentobarbital Sodium**
M. R. KNAPP and H. K. BEECHER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 376–385, Feb. 4, 1956. 18 refs.

In a meticulously controlled trial carried out at the Massachusetts General Hospital (Harvard Medical School), the antiemetic and other systemic effects of dimenhydrinate, chlorpromazine, pentobarbitone sodium, and an inert placebo after nitrous-oxide–ether anaesthesia were compared in 554 cases. The drug or placebo was given intrasmuscularly 10 to 30 minutes before the end of the operation. All of the patients were under continuous observation for 4 hours and 254 for 24 hours after operation, every episode of nausea, retching, and vomiting being recorded. All were interviewed 24 hours after operation and their subjective responses and symptoms noted.

Of 165 patients who received the inert placebo, 58% had nausea, vomiting, or retching during the first 4 hours and 68% during the first 24 hours. After 50 mg. of chlorpromazine (152 cases) the figures were 34% and 45%; and after 150 mg. of pentobarbitone (85 cases) they were 43% and 56% (reduced to 52% when a second dose was given after 4 hours); no reduction in symptoms was observed during the first 4 hours after 100 mg. of dimenhydrinate or 100 mg. of pentobarbitone, but a second dose of the former drug given 4 hours postoperatively was followed by a decrease to 50% of the incidence in the controls. The administration of all three drugs, except pentobarbitone in a dosage of 100 mg., was associated with a very definite increase in the incidence of postoperative hypotension, which in the case of chlorpromazine resisted treatment with the pressor amines.

Patients subjected to intraperitoneal operations showed no increase in the incidence of nausea, retching, or vomiting over the remainder. Females were more likely to vomit than males, the difference being more marked after the first 4 hours; age had no apparent effect. All three drugs caused a significant increase in the time to awakening, the mean figures being as follows: placebo, 87 minutes; dimenhydrinate (100 mg.) or pentobarbitone sodium (100 mg.), 112 minutes; pentobarbitone (150 mg.), 132 minutes; and chlorpromazine (50 mg.), 144 minutes.

It is concluded that reduction in postanaesthetic sickness can be obtained by the administration of 50 mg. of chlorpromazine or 150 mg. of pentobarbitone intramuscularly before the end of the operation, but, it is pointed out, only at the price of delayed awakening, increased risk of hypotension, and, in the case of pentobarbitone, mental confusion and excitement.

Ronald Woolmer

Radiology

RADIODIAGNOSIS

780. **Static Mass Radiography in a London Borough**
G. Z. Brett, B. Benjamin, J. W. Craig, and V. Freeman. *British Medical Journal* [*Brit. med. J.*] **1**, 719–722, March 31, 1956. 8 refs.

In 1952 a mass miniature radiography unit was set up in Islington, a London Metropolitan Borough in which the tuberculosis mortality had been higher than average. During the first 3 years of working 87,261 adults—about one-fifth of the population—were examined, 74,742 of them (86%) for the first time. In this paper the authors analyse this population in regard to social group and prevalence of tuberculosis and bronchial carcinoma; the tuberculosis attack rates were also estimated. As judged by age groups, the proportion of the population radiographed was broadly representative of the total population of the borough, although the proportion of those over the age of 65 was somewhat lower and that of young women somewhat higher. A relatively low proportion of persons in the poorest social circumstances (Registrar-General's Social Class V) came for examination, although this group provided the highest yield of cases of tuberculosis and also contained the highest proportion of sputum-positive cases; surprisingly, this group also had a high incidence of bronchial carcinoma. Generally speaking, the percentage of the population examined decreased with increasing age; a considerable number of those coming for examination were not residents of the borough.

A total of 572 cases of tuberculosis were discovered. Of the males among these, 4% showed minimal disease, 69% moderate disease, and 27% extensive disease, while for females the figures were 15%, 71%, and 14% respectively; 62% of the males and 37% of the females were sputum-positive. The tuberculosis rates were lowest among organized groups (from factories and the like), and highest among patients referred by the local doctors. Over-all, the rate was 7·7 per 1,000, which is more than would be expected from a mobile unit. This higher yield probably resulted from the fact that facilities for radiological examination were continuously available, resulting in an intake from more fruitful sources than organized industrial groups. The rates did not decrease in successive years. The annual attack rate for tuberculosis, estimated from the relatively small number who were examined a second time, was 2 per 1,000, a rate similar to that found by Springett in 1951 (*Brit. med. J.*, 1951, **2**, 144; *Abstracts of World Medicine*, 1951, **10**, 549).

Of bronchial carcinoma, 115 cases were found, a rate of 3·8 per 1,000. In the lowest social group referred to above the rate was 6·3 per 1,000, and among 704 retired men it was 17 per 1,000 (12 cases).

[This is a very interesting and informative paper.]

T. M. Pollock

781. **Basal Horizontal Lines on Chest Radiographs: Significance in Heart-disease**
R. E. Rossall and A. J. Gunning. *Lancet* [*Lancet*] **1**, 604–606, May 5, 1956. 3 figs., 13 refs.

A study was undertaken at the General Infirmary at Leeds to discover whether any relationship existed between the occurrence of the short, horizontal, peripheral, basal lines seen on chest radiographs and either the left auricular or pulmonary arterial pressure. The series comprised 100 patients with mitral valve disease and 16 with pulmonary hypertension arising from other causes. The radiographs were divided into three groups: "lines absent", "lines poor to moderate", and "lines marked". Of the 100 patients with mitral disease, lines appeared on the radiographs of 63; in these, the presence and intensity of the lines were more closely related to the left auricular pressure than to the pulmonary arterial pressure. Of the 16 cases of pulmonary hypertension from causes other than mitral disease, in only 2 did the radiographs contain doubtful lines, and no lines occurred in the remaining 14. In the 5 cases for which measurements of the left auricular pressure were available, these were normal.

It is concluded that: (1) basal horizontal lines on the chest radiographs of patients with mitral disease are associated with a raised left auricular pressure; (2) lines invariably appear when the mean left auricular pressure exceeds 24 mm. Hg; and (3) elevation of the pulmonary arterial pressure alone appears to play little part in the production of lines. They further suggest that the factor responsible for the lines is a rise in pulmonary capillary venous pressure to a level exceeding the colloid osmotic pressure of the plasma proteins; this they regard as indirect evidence for the view that the anatomical basis of the lines is an increase in the bulk of the interalveolar septa.

Sydney J. Hinds

782. **Selective Angiocardiography in Infants and Children**
R. D. Rowe, P. Vlad, and J. D. Keith. *Radiology* [*Radiology*] **66**, 344–361, March, 1956. 18 figs., 11 refs.

The value of selective angiocardiography as a diagnostic procedure in infants and young children is discussed, and the results obtained in 50 patients at the Hospital for Sick Children, Toronto, are described. An hour before the examination the patients received an intramuscular injection of a mixture containing 0·69 mg. of chlorpromazine, 0·69 mg. of promethazine, and 2·74 mg. of pethidine per kg. body weight. A No. 7 or No. 8 cardiac catheter was inserted at the groin under local analgesia, and diodone in a 70% solution was injected rapidly through the catheter under a compressed air pressure of 150 to 200 lb. per square inch (10·5 to 14·0 kg. per sq. cm.). The amount of the contrast medium given was about 1·5 ml. per kg. body weight.

Between 8 and 10 cassettes per second were exposed, a Schönander biplane angiograph being used. In each case an electrocardiogram was obtained at the same time.

The authors' conclusions may be summarized as follows. In patients with the tetralogy of Fallot the right ventricular outflow tract and the site of the right-to-left shunt are clearly demonstrated. Pulmonary stenosis is better studied by cardiac catheterization, but in cases of infundibular stenosis selective angiocardiography may give more precise information about the level and nature of the stenosis. Venous angiocardiography is a satisfactory procedure in infants with transposition of the great vessels, but in older children or in more complicated cases selective angiocardiography may be helpful. In cases of tricuspid atresia the latter may provide more information about the rudimentary chamber and the level of the interventricular defect. In cases of a single ventricle it may be impossible to decide by venous angiocardiography whether this anomaly exists. Finally, with selective angiocardiography it is possible in cases of isolated interventricular defect with a high right ventricular pressure to show the size and position of the defect.

It is concluded that while venous angiocardiography is helpful in very small infants with cyanotic heart disease, selective angiocardiography is of special value in those cases in which the broad anatomy of the defect is suspected, but particularly clear visualization of a certain area is required. *John H. L. Conway-Hughes*

783. **Roentgen Aspects of Atrial Septal Defects, Ostium Secundum.** [In English]
W. F. KRAEMER, G. GENSINI, S. G. BLOUNT, and R. R. LANIER. *Acta radiologica* [*Acta radiol.* (*Stockh.*)] **44**, 441–450, Dec., 1955. 9 figs., 6 refs.

The authors discuss briefly the pathology of atrial septal defect, which in their experience is the most common type of congenital malformation of the heart, the ostium secundum type being the most important, constituting more than 95% of all cases of atrial defect seen at the University of Colorado Medical Center, Denver. Exact diagnosis is of the utmost importance as these cases are suitable for surgical repair—during the past 2½ years the authors have carried out such an operation under direct vision in 20 cases. An attempt is therefore made to estimate the diagnostic value of the radiological findings in these 20 cases.

Vascularity of the lungs was found to be increased in all cases. The main pulmonary artery was also increased in size in all cases, as were the right and left pulmonary arteries. The size of the heart was consistently increased owing to enlargement of the right atrium and right ventricle, the pulsation of the latter being increased. The size of the left heart was within normal limits in all cases. However, there was a marked lack of correlation of these findings with each other and with the haemodynamic factors, and it is concluded that it is often impossible to distinguish this condition from other types of left-to-right shunt at the atrial level and from interventricular shunts by radiological methods alone.
M. E. Grossmann

784. **Radiological Signs of Rheumatoid Arthritis. A Study of Observer Differences in the Reading of Hand Films**
J. H. KELLGREN. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **15**, 55–60, March, 1956. 14 refs.

Since defined gradings of the radiological changes in the hands and feet in rheumatoid arthritis are being used as diagnostic aids in epidemiological studies and large-scale therapeutic trials, some knowledge of the extent of variation in interpretation of the same films by different observers and of the reproducibility of *x*-ray gradings by any given individual is desirable. The author therefore used 3 sets of radiographs of the hands in an attempt to estimate the range of variation to be expected between the interpretations of different observers and those of the same observer on different occasions. The first set consisted of 192 films of the hands in cases of definite early rheumatoid arthritis, and these were independently interpreted by 6 experienced observers, 4 being clinicians and 2 radiologists, one of the former reading the films a second time. The second set consisted of 126 films of the hands of patients aged 55 to 64 with some clinical or other evidence suggestive of rheumatoid disease; these were read 3 times by a single observer, the combined grading for rheumatoid arthritis being recorded on the first and second occasions, and erosion and porosis being graded separately at the third. The third set consisted of 259 films of the hands in cases of clinical polyarthritis; these were read twice by a single observer at an interval of over a year.

Wide disagreement between the 6 observers was noticeable in the recognition and assessment of osteoporosis, and although erosion was diagnosed with reasonable certainty, its severity was variably interpreted. Comparison of the gradings for rheumatoid arthritis with those for porosis in the second set showed wide disagreement, whereas there was good agreement with those for erosion. Re-assessment of the third set after a year showed only small differences in the readings.

The author suggests that an agreed set of standard reference films should be used for the assessment of comparative prevalence rates by different observers. Where radiographs are used for assessment of progress in therapeutic trials the reading of all films should be made by the same observer, preferably at a single session.
M. E. Grossmann

785. **Anterior Displacement of the Descending Duodenum as an Aid in the Diagnosis of Retroperitoneal Tumor**
E. J. GANEM, D. W. WALLWORK, and G. V. WEST. *New England Journal of Medicine* [*New Engl. J. Med.*] **254**, 552–555, March 22, 1956. 7 figs., 13 refs.

An adrenal tumour may be visible as a soft-tissue mass on a plain radiograph of the abdomen, and pyelography may reveal displacement of the kidney by the tumour. Alternatively, various more specialized procedures may be used, including tomography, retroperitoneal pneumatography, and aortography. When the left adrenal gland is involved gaseous distension of the stomach is advocated to eliminate confusing shadows; in some instances tumours of the left adrenal gland may also displace the

stomach forward. In this paper from the General Hospital, Lawrence, Massachusetts, the radiological appearances in a case of carcinoma of the right adrenal gland are described.

A man aged 50 had had pain in the right upper portion of the abdomen for a year. A barium-meal examination revealed a prepyloric peptic ulcer; this healed under medical treatment. The patient still complained of pain, however, and at a third *x*-ray examination 8 months after the first there was anterior displacement of the second part of the duodenum, visible in the right lateral recumbent position. This displacement became progressively more marked over a period of 15 months. Intravenous and retrograde pyelograms were considered to be normal. Exploration revealed a carcinoma of the right adrenal gland displacing the duodenum anteriorly. After removal of the carcinoma, the patient became free from pain, but metastases developed later.

The authors point out that the second part of the duodenum is attached to the anterior surface of the right kidney and is sometimes also an anterior relation of the base of the right adrenal gland, as it lies in contact with the upper pole of the kidney. In the latter case adrenal enlargement might be expected to displace the second part of the duodenum forward, and this can best be demonstrated in radiographs taken with the patient in the left lateral recumbent position. Normally, in this position, the second part of the duodenum overlaps the vertebral column. *G. Ansell*

786. **Basic Combined Cholecystangiography**
D. J. MITCHELL. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 133–138, March, 1956. 7 figs., 8 refs.

The radiographic investigation of the biliary ducts and gall-bladder with " biligrafin " by intravenous injection may entail repeated examinations of the patient over a period of several hours. While biligrafin is much more reliable than other media for the demonstration of the ducts, visualization of the gall-bladder alone can be achieved equally well with the oral preparation " telepaque " (iopanoic acid). In order to reduce the time required for cholecystangiography the author, working at the Royal Albert Edward Infirmary, Wigan, has developed a combined method, using telepaque to demonstrate the gall-bladder and biligrafin to demonstrate the duct system, both being visualized simultaneously.

The procedure is as follows. After a fat-free evening meal the patient takes 3 g. of telepaque and is radiographed. A further radiograph is taken 11 hours later, followed by the intravenous injection of 20 ml. of biligrafin. After 30 minutes another radiograph is taken, a fatty meal is then given, and the final film is exposed 30 minutes later. If the gall-bladder is not visualized in the first or second film a further injection of 20 ml. of biligrafin is given. No evidence of incompatibility of the two media has been found, the only reactions noted being occasional nausea or retching after the injection of biligrafin.

This basic technique was used in 100 unselected cases of dyspepsia thought to be of biliary origin and the result was considered satisfactory in at least 95. The gall-bladder was adequately filled 11 hours after the ingestion of telepaque in 72 cases, and in 12 of the remainder satisfactory filling was obtained 30 minutes after the injection of biligrafin. The cystic duct was visualized in 88 cases, the hepatic duct in 98, and the common bile duct in 99 (the single exception being in a very obese subject). It was found that the ducts were best visualized 30 minutes after the injection of biligrafin in 67 cases, and after the fatty meal in 32 cases. Calculi were detected in 19 cases, being confined to the ducts in 9.

The author claims the following advantages for the method: (1) demonstration of the complete biliary tract in a high proportion of cases; (2) economy of time, the examination usually being concluded within one hour; (3) economy of film, which usually offsets the small extra cost of using two contrast media; and (4) reduction in the need for operative cholangiography and exploration of the ducts in some cases. *R. Murray*

787. **Interpretation of the Intravenous Cholangiogram**
R. E. WISE and R. G. O'BRIEN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **160**, 819–827, March 10, 1956. 6 figs., 15 refs.

Intravenous cholangiography with sodium iodipamide (identical with " biligrafin ") as the contrast medium was carried out at the Lahey Clinic, Boston, in 300 cases, in 191 of which the gall-bladder had been removed. None of the patients was asymptomatic. Duct shadows were seen in 82% of the post-cholecystectomy cases and in 88% of those with intact gall-bladder. The degree of opacification was correlated with biochemical findings in a number of cases. The serum bilirubin level and the results of the " bromsulphalein " retention test proved to be of little value in predicting the type of shadow.

Reactions to the injection, which were relatively mild, were noted in 34 (11·3%) of the 300 cases. In 142 of the cases in which the gall-bladder had been removed the diameter of the common bile duct was measured on the radiograph in order to correlate this with subsequent surgical evidence of the presence or absence of obstruction. In the group in which obstruction was found the diameter varied from 8 to 30 mm.; in the unobstructed group the range was 3 to 15 mm. The degree of overlap thus rendered the measurement of the duct diameter of little value in the diagram of obstruction.

The authors, seeking a more useful criterion, noted that there was marked variation in the duration of opacification of the common bile duct. In one group of 38 cases in which the duct, but not the gall-bladder, was seen, owing either to absence of the latter or its failure to fill with dye, a high degree of correlation was observed between the length of time the contrast medium remained in the duct and the subsequent finding of an obstruction. The authors now base a diagnosis of partial obstruction on the presence of the medium in the duct in a concentration at 120 minutes not appreciably less than that at 60 minutes. If the gall-bladder is present and visible the estimate is not valid, since the distensible reservoir of the gall-bladder will operate to retain opacity in the common duct for an indefinite period in the absence of any obstruction.

The nature of the bile-duct obstruction is not always discernible. In 14 cases of proved calculus obstruction the actual stones were visible radiologically in 7. Fibrosis of the sphincter of Oddi was found in 6 of the 14 cases and in 3 of the 6 a radiological diagnosis of obstruction had been made without detecting calculi.

The authors carry out intravenous cholecystography in all cases in which there is failure to visualize the gall-bladder after oral administration of the dye. In 12 out of 34 such cases a gall-bladder shadow was demonstrated on subsequent intravenous cholecystography.

A. M. Rackow

788 (*a*). **Hypaque in Intravenous Pyelography. An Analysis of 50 Controlled Examinations Comparing Hypaque with 50 per cent. Diodone**

B. C. HALE. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 158–160, March, 1956. 6 refs.

788 (*b*). **A Comparative Study of the Value of Sodium Acetrizoate (Diaginol) 50 per cent. and Sodium Diatrizoate (Hypaque) 45 per cent. in Intravenous Urography**

B. GREEN and J. G. SOWERBUTTS. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 161–165, March, 1956. 9 figs., 14 refs.

788 (*c*). **Report on 1028 Cases of Intravenous Urography with Sodium Acetrizoate (Diaginol) as Contrast Medium**

P. CAVE, G. A. BURFIELD, and J. A. RANKIN. *British Journal of Radiology* [*Brit. J. Radiol.*] **29**, 166–168, March, 1956. 9 refs.

Two new contrast media for excretion pyelography, "diaginol" (sodium acetrizoate) and "hypaque" (sodium 3:5-diacetamido-2:4:6-triiodobenzoate), both contain 3 atoms of iodine in each molecule and therefore have a higher degree of radio-opacity than diodone, the molecule of which contains only 2 iodine atoms. The iodine content of diaginol is 65·8% and of hypaque 59·8%, compared with 48·9% for diodone.

The first of these papers, from the Middlesex Hospital, London, describes the pyelographic findings in 50 cases after the injection of 20 ml. of 45% hypaque. These patients had all been examined previously with 50% diodone within a period of 18 months, and when asked to express their preference 33 chose hypaque and only one diodone, the other 16 patients having no particular preference. Objectively, the number and severity of reactions were significantly less with hypaque, but one patient reacted to hypaque although she had not previously reacted to diodone. Hypaque was usually excreted more rapidly than diodone and produced significantly better pyelograms.

The second paper, from St. Bartholomew's Hospital, London, and the London Hospital, describes the pyelographic findings with sodium acetrizoate in 250 cases and with hypaque in 500 cases. Those patients who had previously received diodone again mostly expressed a preference for the newer drugs. A considerable number of the patients who received sodium acetrizoate experienced pain in the arm or shoulder due to venous spasm, and flushing, vomiting, and tingling occurred more frequently than with hypaque; the incidence of other types of general reaction, however, was not significantly different in the two groups. When hypaque was injected in not less than 30 seconds and not more than 60 seconds there was a significant decrease in the incidence of reactions. The degrees of contrast produced by the two media were similar, but the rate of excretion of hypaque was slightly the more rapid. Visualization of the lower ureters was best when abdominal compression was not used, but the application of abdominal compression 5 minutes after the injection improved the visualization of the renal pelvis, calyces, and upper ureter. It is concluded that owing to the lower incidence of reactions hypaque is the more acceptable of the two for general use.

The third paper, from the Royal Berkshire Hospital, Reading, compares the findings obtained with 30%, 50%, and 70% solutions of sodium acetrizoate in 273, 549, and 206 cases respectively. The most useful pyelograms were obtained with 70% solution, though those obtained with the 50% solution were almost as good. The 30% solution was, however, significantly less satisfactory. On the other hand the 70% solution tends to crystallize out, which may interfere with the injection, and also gave a slightly higher incidence of side-reactions. It is therefore considered that 50% is the most suitable concentration of sodium acetrizoate for routine intravenous urography.

G. Ansell

RADIOTHERAPY

789. **Cancer of the Floor of the Mouth**

A. RAHAUSEN and C. SAYAGO. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **75**, 515–518, March, 1956. 6 refs.

The authors report 40 cases of carcinoma of the floor of the mouth which were treated at the Radium Institute, Santiago, Chile, between 1930 and 1949. These cases probably represent the total incidence of the disease in that country and constituted 7·7% of all cases of cancer of the lip and mouth treated during the period. All but 2 of the patients were male. There were 37 cases of epidermoid carcinoma, 2 of undifferentiated carcinoma, and one of sarcoma. Lymph-node metastases were present in 5 cases when first seen and developed subsequently in 6 others—a total incidence of 27·5%.

Most of the cases were treated by the interstitial implantation of radium, with external irradiation by means of a submental radium mould also in some. In a number of more advanced cases *x*-ray treatment was used. So far as surgery is concerned, the authors consider that "the only justified procedure is the 'en bloc' resection of the tumor plus the adjacent portion of the tongue and removal of half of the mandible". They usually perform prophylactic block dissection of the lymph nodes, mainly because their patients do not attend regularly for follow-up examination. Six patients (15·7%) survived 5 years, all of whom were treated with radium. The authors regard the optimum dose as 7,000 r in 8 days. No patient with invasion of the gum or lymph-node metastases survived.

John Boland

790. **Supervoltage Roentgen Therapy in Cancer of the Lung**
T. A. WATSON. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **75**, 525–529, March, 1956. 1 fig.

The author reviews the fate of 611 cases of cancer of the lung (61% histologically proved), seen at the Saskatchewan Cancer Clinics between 1932 and 1953, in relation to the type of treatment given. Of 54 patients who underwent radical surgery, 17 are alive, whereas of 108 who underwent thoracotomy alone or combined with non-surgical treatment, only 8 are alive. In 319 cases no treatment was possible, and the remainder received *x*-ray therapy or nitrogen mustard, or both.

There was little difference in average survival time between the untreated cases and those having conventional *x*-ray therapy, though many of the latter showed subjective and radiological improvement. Treatment by radioactive cobalt beam or 23-MeV betatron not only resulted in improvement in most cases, but gave a longer average survival. Of 28 patients treated with the betatron, 5 are still alive, the average survival being 20 months. Nitrogen mustard, when combined with conventional *x*-ray therapy, increased the average survival time. The author concludes that supervoltage therapy seems to offer nothing curative, but suggests the combination of supervoltage and nitrogen mustard treatment to obtain the best palliation.

John Boland

791. **The Intensive Divided-dose Irradiation Therapy of Carcinoma of the Uterine Cervix: Rationale and Late Results**
R. E. FRICKE and D. G. DECKER. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **75**, 502–507, March, 1956. 2 refs.

The authors describe in detail the technique employed at present at the Mayo Clinic for the treatment of carcinoma of the uterine cervix with radium. One 50-mg. tube of radium is inserted twice weekly for 4 weeks, each insertion lasting 10 to 14 hours except for the 5th insertion, when two such tubes are used in tandem in the uterus and remain in position 20 to 24 hours. The dose to Point A is stated to be at least 7,000 gamma roentgens and to Point B at least 2,000 gamma roentgens. *X*-ray therapy is given to the lateral parametria over the whole of this period except on the day of the 5th insertion. [For further details the reader is referred to the original article.] (In recent years a few selected young patients with Stage-I and -II lesions have undergone Wertheim's hysterectomy 3 months after the above treatment, but this is still regarded as being on a trial basis.)

The advantages claimed for this form of treatment are that a homogeneous dose of radiation is given to the birth canal, the cervix is not dilated more than is necessary for insertion of the radium tube, which is only 4 mm. in diameter, and difficulties such as the presence of a tumour filling the vagina, infection, and haemorrhage can easily be met by modifying the treatment without departing from the basic aim of irradiating fully all the tissues potentially affected. All the radium insertions are carried out with the patient in the knee–chest position to facilitate adequate exposure; no anaesthetic is given and the patient is in hospital for only about 24 hours for each insertion. The fact that she is ambulant for the remainder of the treatment helps to maintain the patient's morale.

From 1940 to 1948 1,309 cases were treated, 63·4% with radium and *x*-ray treatment, 10·1% with radium alone, and 10·6% with surgery alone. The remainder had a combination of two or more forms of treatment. Five-year survival figures are shown against Broder's grading of the tumours, the results varying from 69·6% for Grade II (no cases of Grade I are reported) to 53·5% for Grade IV. Of the 1,059 patients treated by irradiation, 964 were followed up for 5 years, and of these 51·7% were alive. Assuming that the 95 patients lost to follow-up all died of cancer the 5-year survival rate becomes 47·0%, which compares well with the corresponding figure in the last report from the same clinic, which was 32·8%.

J. M. Gibson

792. **Treatment of Endometrial Adenocarcinoma. A Study of 381 Cases at the New York Hospital**
C. T. JAVERT and R. G. DOUGLAS. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **75**, 508–514, March, 1956. 11 refs.

Between September, 1932, and December, 1954, 365 patients with endometrial carcinoma were treated at the New York Hospital (Cornell University Medical College), 161 by surgery alone, 178 by surgery with pre- or post-operative radium or *x*-ray therapy, and 26 by irradiation alone. No treatment was possible in a further 16 cases. Thus the condition was considered to be operable in 339 cases.

The distribution of cases according to both clinical and surgico-pathological staging systems is shown, and it is noted that whereas in the years 1932–46 only 5 cases were seen in which the lesion was limited to the endometrium (Stage O), in the years 1947–54 30 such cases were seen. The authors suggest that this is due to the wider use of smear examinations for diagnosis during the latter period. Since 1947, 16 patients have undergone radical lymphadenectomy as part of the treatment and 61 selective or incomplete lymphadenectomy. Only one patient with lymph-node metastases has lived over 5 years out of 185 followed up for that period. The authors emphasize the high frequency of blood-borne metastases in this disease, especially when the pelvic lymph nodes are involved. They consider vaginal metastases to be blood-borne and of serious prognostic importance, since in over 80% of such cases the patient died in less than 5 years. The over-all 5-year survival rate for the 185 cases followed up for that period was 65·4%. This figure is compared with Heyman's figure of 61·8% for primary radium therapy alone [but should have been corrected to 64% to allow for the exclusion of Stage-O cases from Heyman's series].

[The results are not analysed according to the various forms of treatment used, nor is the choice of treatment for any particular patient discussed; and although the

authors present their arguments against the routine pre-operative use of radium as a summary of the article, these form an independent statement of opinion rather than natural conclusions to be drawn from the material in the report.] *J. M. Gibson*

793. **Comparative Radiotherapeutic Results in Carcinoma of the Endometrium as Modified by Prior Surgery and Post-irradiation Hysterosalpingo-oophorectomy**
H. B. HUNT. *Radiology* [*Radiology*] **66**, 653–666, May, 1956. 5 figs., 36 refs.

794. **Selective Irradiation of Lymph Nodes by Interstitial Injection of Radioactive Colloidal Gold**
H. F. BERG and W. M. CHRISTOPHERSON. *American Surgeon* [*Amer. Surg.*] **22**, 172–178, Feb., 1956. 6 figs., 8 refs.

The selective irradiation of lymph nodes by interstitial injection of radioactive colloidal gold (^{198}Au) was attempted in a number of experiments at the University of Louisville School of Medicine, Kentucky. When colloidal particles ranging in size from 0·003 to 0·004 microns are injected into the tissues they are carried to, and remain concentrated in, the lymph nodes draining the site of the injection. In the present experiments ^{198}Au was injected directly into the urinary bladder, the bronchial mucosa, and the superior mammary gland of dogs. The primary site and the lymph nodes were then examined, autoradiographs being taken of the latter after suitable intervals. Areas of radiation damage were found.

It is pointed out that the local tolerance at the injection site, the time taken for the isotope to reach the lymph nodes—which must obviously be short in relation to the half-life of the isotope (2·7 days)—and the distance of the injection site from the lymph nodes are the main factors influencing the efficacy of this method of irradiation. The concentration of radiation in the lymph nodes was found to vary with the amount of isotope given and to be patchy in distribution. This last factor, together with the tolerance limits at the injection site, are the main obstacles to the use of this method in clinical radiotherapy. *R. D. S. Rhys-Lewis*

795. **Prevention and Treatment of Radiation Leucopenia by Means of Injections of Suspensions of Leucocytes.** (Опыт применения лейкоцитной взвеси в борьбе с рентгеновской лейкопенией)
E. D. DUBOVÏI, E. L. SHVARTSMAN, G. A. FOÏGEL', and R. S. ROMANYUK. *Вестник Рентгенологии и Радиологии* [*Vestn. Rentgenol. Radiol.*] 25–28, No. 2, March–April, 1956. 3 figs.

The authors state that radiation leucopenia may be prevented by the injection of leucocytes obtained from stored blood, where they are concentrated in the whitish layer (" buffy coat ") which lies above the mass of the erythrocytes. This layer contains about 100,000 to 150,000 leucocytes and about 1,500,000 to 2,000,000 thrombocytes per c.mm.

Altogether, 37 patients have been treated by this method, in 5 of whom leucopenia was already present before radiotherapy. The age of the stored blood was 3 to 4 days, and about 10 to 20 ml. of the leucocyte suspension separated from the rest of the blood was injected either intravenously or intramuscularly, the injection being repeated at intervals of 2 to 7 days during treatment with *x* rays.

It was observed that in all the cases treated the leucocyte count either increased or remained stationary in spite of radiotherapy. In some cases there was an absolute increase in the lymphocyte count, and in cases of thrombocytopenia there was also an increase in the number of circulating thrombocytes. *A. Orley*

796. **A Study of the Effectiveness of Pyridoxine and Dramamine on Clinical Radiation Sickness**
A. SILVERMAN, M. M. KLIGERMAN, J. W. FERTIG, and K. ELLIS. *Radiology* [*Radiology*] **66**, 403–407, March, 1956. 1 fig., 2 refs.

The authors, from the College of Physicians and Surgeons (Columbia University) and the Presbyterian Hospital, New York, describe a statistically controlled study of the value of " dramamine " (dimenhydrinate) and pyridoxine in radiation sickness. Four sets of capsules identical in appearance were made up with the following contents, which were known only to the pharmacist: (1) pyridoxine, 25 mg., and dimenhydrinate, 50 mg.; (2) lactose (placebo); (3) pyridoxine, 25 mg.; (4) dimenhydrinate, 50 mg. Over one year all patients (to a total of 185) being treated definitively by irradiation at an H.V.L. of 1·0 to 1·5 mm. Cu were given three tablets daily during their period of radiotherapy. Patients were divided into 9 groups by anatomical site (abdomen, chest, extremities) and over-all time of treatment (8 to 10 days, 2 to 3 weeks, 4 to 6 weeks), and the capsules were assigned at random to each group. The physician treating the patient recorded daily his assessment of the degree of radiation sickness in four grades of severity (0, 1, 2, and 3).

Of the 185 patients, only 2, both of whom were having abdominal irradiation, had Grade-3 sickness; 12 patients had Grade-2 sickness, 7 of these receiving abdominal treatment. Taking all grades together, radiation sickness was noted in 38 (57·6%) out of 66 given abdominal irradiation, in 34 out of 73 (46·6%) receiving thoracic irradiation, and in 13 out of 46 (28·3%) given treatment to the extremities. The authors conclude that the number of patients with radiation sickness of Grades 2 and 3 was so small that comparison of the effectiveness of the different capsules in preventing severe sickness is meaningless. With the χ^2 test no statistically significant difference could be found between the effects of any of the capsules. A graph shows the percentage of sick patients in each group on any day of treatment; the authors note that there was usually a delay of 7 to 10 days before sickness began, and some patients became asymptomatic in spite of continued treatment.

No conclusions were reached concerning the effect of over-all duration of treatment, it being pointed out that this tended to vary directly with the site treated and the number of portals used. *E. D. Jones*

History of Medicine

797. **Longevity and the Early History of the Tetralogy of Fallot**
R. M. MARQUIS. *British Medical Journal* [*Brit. med. J.*] **1**, 819–822, April 14, 1956. 6 figs., 37 refs.

The early history of the tetralogy of Fallot is reviewed. Attention is directed to the original description of the malformation in 1673 by the Danish anatomist Nicolas Steno. The important contribution to contemporary knowledge by British physicians of the 19th century is stressed.

Two cases which came to necropsy when the patients were 65 and 48 years of age respectively are reported in full. They bring to 12 the total number of recorded cases of the tetralogy of Fallot in which the patient survived to 40 years of age. The patient in the first case is the oldest female with the tetralogy recorded.—[Author's summary.]

798. **Historical Notes on the Iconography of the Heart.** [In English]
A. SCHOTT. *Cardiologia* [*Cardiologia (Basel)*] **28**, 229–268, 1956. 22 figs., bibliography.

This review of some of the stages in the development of the iconography of the heart reflects human progress in knowledge of this organ and its functions. In the Arabian period the first illustrated monograph on anatomy, published in Persia, was the *Illustrated Anatomy* of Mansur (1396). In the Wellcome Historical Medical Library, London, is an illustration of the venous system, which is unquestionably a copy of an analogous illustration in Mansur's book. This drawing might be expected to contain much based on Galen's conceptions, but in fact it contains surprisingly little. Indeed, it is a highly imaginative representation, although the drawing of the heart is acceptable as far as its external shape is concerned except for the exaggerated size of what appear to be the auricles.

An early example of occidental anatomical illustration is to be found in the *Fasciculus Medicinae* of Johannes de Ketham (1491). This contains a drawing of a pregnant woman in which, however, no attempt is made to show the normal position of organs or to illustrate any of Galen's ideas, with one exception—namely, that the trachea is shown connecting the mouth with the heart. In Leonardo da Vinci's earlier drawings the heart is seen as a two-chambered organ and, in keeping with Galen's teaching, the veins are emphasized more than the arteries. Later in life Leonardo established, as a result of his own researches, that the heart has four chambers and he also accurately drew the human thoracic aorta and its branches. In the illustrations in the works of Vesalius the branching of the aorta is like that found in apes and the caval system is represented as forming one vessel. Eustachius, a contemporary of Vesalius, possessed anatomical plates, which were lost until Lancisi found them 150 years later in the Vatican Library and published them (1714). The Eustachian illustrations show the valve named after him, as well as the valve of the coronary sinus which had been described by and named after Thebesius in 1708. Lancisi's 1722 edition of Eustachius's works shows that the great anatomist also correctly depicted the branches of the aorta.

Lower, in his *Tractatus de Corde* (1669), illustrates the tuberculum intervenosum (of Lower) and the branches of the aorta, and discusses the dynamics of blood flow through the aorta and its branches. Ruysch, who is credited with being the discoverer of a method of injecting blood vessels in the cadaver, in his *Thesaurus Anatomicus* (1704) clearly demonstrates the ramifications of the coronary arteries, and Albrecht von Haller includes in his *Icones Anatomicae* (1749) a drawing of the heart of a female infant and adds a number of annotations on the figure.

Towards the end of the eighteenth century the combination of brilliant anatomist and superb artist is found in the person of Antonio Scarpa, whose *Tabulae Nevrologicae* (1794) contain illustrations " admirably expressive of the subject ", including one of the carotid sinus. Progress in the nineteenth century is revealed in the works of Paolo Mascagni and Richard Quain, the illustrations in which are in colour. The first half of the nineteenth century " appears to be distinguished by an advance on the artistic side, rather than by much progress in the accurate anatomical representation of the heart which had been achieved previously ".

H. P. Tait

799. **Handwashing and the Eyesight in the *Regimen Sanitatis***
R. LOEWE. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **30**, 100–108, March–April, 1956. Bibliography.

800. **The British Medical Council and British Medical Education in the Nineteenth Century**
A. BECK. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **30**, 150–162, March–April, 1956. Bibliography.

801. **The Romantic Period in Medicine**
I. GALDSTON. *Bulletin of the New York Academy of Medicine* [*Bull. N.Y. Acad. Med.*] **32**, 346–362, May, 1956.

802. **The Influence of Edwin Chadwick on American Public Health**
H. WILLIAMS. *Medical Officer* [*Med. Offr*] **95**, 273–279, May 25, 1956. Bibliography.

803. **Dr. Edith Pechey, one of the First Women in Medicine**
S. D. MEARES. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 951–954, June 9, 1956. 1 fig., 17 refs.